"EVALUATION OF HYPERBILIRUBINEMIA AS A NEW DIAGNOSTIC MARKER FOR ACUTE APPENDICITIS AND ITS ROLE IN THE PREDICTION OF APPENDICULAR PERFORATION"

A DISSERTATION SUBMITTED TO

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In partial fulfilment of the regulations for the award of the

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DECLARATION

*I Dr.D.Chandrasekaran solemnly declare that this dissertation titled "***EVALUATION OF HYPERBILIRUBINEMIA AS A NEW DIAGNOSTIC MARKER FOR ACUTE APPENDICITIS AND ITS ROLE IN THE PREDICTION OF APPENDICULAR PERFORATION***" is a bona fide work done by me in the Deparment of General Surgery,Govt.Stanley Medical College and hospital, Chennai under the supervision of*

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This dissertation is submitted to the Tamilnadu DR MGR Medical University, Chennai in partial fulfilment of the university regulations for the award of M.S degree(General Surgery),branch-1 examination to be held in April 2015.

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CERTIFICATE

*This is to certify that the dissertation entitled "***EVALUATION OF HYPERBILIRUBINEMIA AS A NEW DIAGNOSTIC MARKER FOR ACUTE APPENDICITIS AND ITS ROLE IN THE PREDICTION OF APPENDICULAR PERFORATION***" is a bona fide work done by DR.Chandrasekaran.D post graduate(2012-2015) in the department of general surgery, Govt .Stanley Medical College and hospital,Chennai under my direct guidance and supervision, in partial fulfilment of the regulations of the Tamilnadu Dr.Mgr medical university Chennai for the award of M.S degree(General surgery) Branch-1 examination to be held in April 2015*

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CONTENTS

LIST OF ABBREVIATIONS USED

ALP - Alkaline phosphatase

ALT - Alanine transaminase

AST - Aspartate transaminase

ATP - Adenosine triphosphate

cm - Centimeter(s)

CRP - C-reactive protein

CT - Computed tomography

dL - Deciliter(s)

DLC - Differential leukocyte count

E. Coli - Escherichia coli

ELISA - Enzyme linked immunosorbent assay

g - Gram(s)

HbsAg - Hepatitis B surface antigen

IL-6 - Interleukin-6

LFT - Liver function tests

mg - Milligram(s)

mL - Milliliter(s)

mm - Millimeter(s)

n - Total number

NPV - Negative predictive value

OR - Odds ratio

PPV - Positive predictive value

SB - Serum bilirubin

SGOT - Serum glutamic oxaloacetic transaminase

SGPT - Serum glutamic pyruvic transaminase

SMV - Superior mesenteric vein

Sr. - Serum

TLC - Total leukocyte count

TNF - Tumor necrosis factor

TSB - Total serum bilirubin

USG - Ultrasonography

WBC - White blood cells

INTRODUCTION

The most common cause of acute abdomen is Appendicitis. The diagnosis of acute appendicitis is based on clinical history and physical examination. It is difficult to diagnose in cases of retrocaecal or retro ileal appendix. Appendicectomy is the most commonly performed abdominal surgery. 15-30% of appendicectomy specimen found to be normal.In order to decrease the number of unnecessary appendicectomy, significance of labarotory investigations like White Blood Cells,,C-Reactive Protein, etc have been emphasised.Ultrasonagram abdomen has been widely accepted as the diagnostic tool for appendicitis.Many number of scoring system were developed to arrive the diagnosis.These scoring systems are based on clinical features,laboratory investigations.Some examples are Alvarado,Modified alvarado,Ripasa.

Still there is no definitive laboratory marker for acute appendicitis and appendicular perforations. Studies show that serum bilirubin is raised in acute appendicitis and appendicular perforations.But the siginificance of which is not stressed.On bacterial invasion of the appendix, there is transmigration of bacteria and release of proinflammatory cytokines like TNF α,.IL6 .

The cytokines reach the liver through the superior mesentric vein and may lead to inflammation, abscess and liver dysfunction.

In view of the above context, the present study was undertaken to assess the relationship between HYPERBILIRUBINEMIA and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

OBJECTIVES

The objectives of the study were-

1. To study the relationship between hyperbilirubinemia and acute appendicitis; and to evaluate its credibility as a diagnostic marker for acute appendicitis.

2. To evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

REVIEW OF LITERATURE

HISTORY

For many years, the appendix was erroneously viewed as a vestigial organ with no known function. It is now well recognized that the appendix is an immunologic organ that actively participates in the secretion of immunoglobulins, particularly immunoglobulin A (IgA)[23].

The history of the appendicitis is present since the history of medicine, apparently the disease of appendix existed in ancient times with fibrous adhesions in the right lower portion of the abdominal cavity being found in an Egyptian mummy from the Byzantine era (Elliot, Smith and Derry).

The appendix was probably observed by both Egyptian and Arabic anatomists in ancient times. Da Vinci used the Arabic term “Orecchio” (Literally ear) to describe the vermiform appendix of the caecum.

There is also, the mention of “Affliction of Appendix”, by Sushruta in his “Samhita” approximately 2500 years ago (P. Kutumbaiah, Ancient Indian Medicine).

The famous Pathologist Reginald Webber Fitz (1843-1913) was the first man to establish acute appendicitis as a definitive lesion and he also explained the relationship of peritonitis as a result of acute appendicitis which was ill-understood till then[26].

Menon of India in 1928 cited that the lymphocytes are normally found in considerable numbers in the submucosa. He felt that a definite relationship existed between the lymphoid hyperplasia of the appendix and the colic like pain in the abdomen.

Surgery

The first appendicectomy was done in saint. George’s Hospital, London, in 1736 by Claudius Amyand, a surgeon at St. George's Hospital in London and Sergeant Surgeon to Queen Ann, King George I, and King George II. The acutely inflamed appendix, perforated by a pin, and surrounding omentum was removed through a scrotal wound while dealing with a faecal fistula in a chronic scrotal hernia. The patient was 11-year-old boy and patient recovered.[2,23,27]

The first published account of appendicectomy for appendicitis was by Krönlein in 1886. However, the patient died on second postoperative day.

Charles McBurney (1845-1913) was one of the surgeons pioneering the diagnosis and operative treatment of appendicitis. Muburneys work on early intervention in acute appendicitis was presented in New York Surgical Society in the year of 1889. Maximum abdominal pain in appendicitis,now known as Mcburneys point had been described during this society meeting.[28]

Five years later in 1894, he set forth in another paper the incision that he used in cases of appendicitis, now called McBurney‟ s incision.[28]

However, McBurney later credited McArthur with first describing this incision.[28]

The surgeon of united states,Murphy had done early appendectomy in equivocal cases of appendicitis. In 1904, he advanced the well known dictum "in case of acute appendicitis open the abdomen as quickly as possible and close it, more quickly". He described the triad of pain abdomen, vomiting and fever, which remains a sound basis for diagnosis even today.[29]

Dawbarn suggested the use of a purse string suture, placed around the base of the appendix. 1889, Senn first noticed and reported the ligature slip and its further complication of peritonitis.

Kurt Semm performed the world's first lap. appendicectomy at the Kiel University, Germany, On 13 September 1983

Laparoscopic appendicectomy is now as widely used as Open appendicectomy and their comparison has been a matter of great debate.

EMBRYOLOGY AND DEVELOPMENT

Around the beginning of the sixth week of development of embryo, the vermiform appendix and the Caecum develops from the caecal bud which arises from the antimesenteric borders of the caudal limb of the mid gut loop[2]. At this stage definite identification of the small and large intestine as separate entities occur. The out pouching maintains a conical shape until the fifth month of fetal growth, after which proximal portion expands to form the Caecum and the tip begins to elongate and develops into the vermiform appendix[31].

About two weeks after birth, lymphoid tissue first appears in human appendix. The number of lymph follicles gradually increases to a peak of about 200 between the ages of twelve and twenty. After thirty there is an abrupt reduction to less than half and then to trace or total absence of lymphoid tissue after sixty.

CONGENITAL ABNORMALITIES:

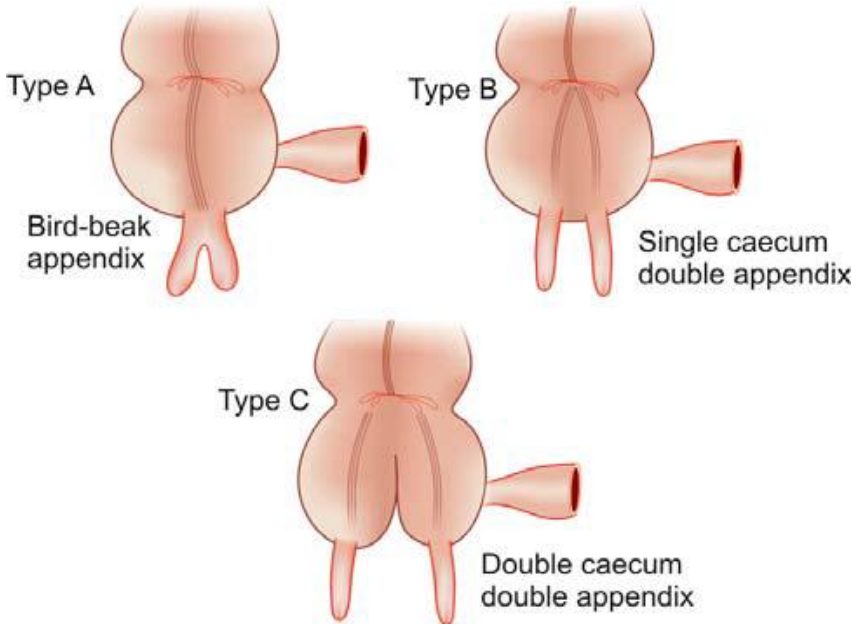
DUPLICATION OF APPENDIX

(Wallbridge Classification)

Type A: Partial duplication in a single caecum.

Type B: Two separate appendices in a single caecum.

Type C: Double caecum with each one having one appendix.



DUPLICATIONS OF APPENDIX

Various positions of appendix:

_ Most common position *is retrocaecal (75%).*

Next common is pelvic (21%).

Other sites are:

_ Preileal—rarest (1%)

_ Postileal

_ Paracaecal

_ Subcaecal

_ Subhepatic

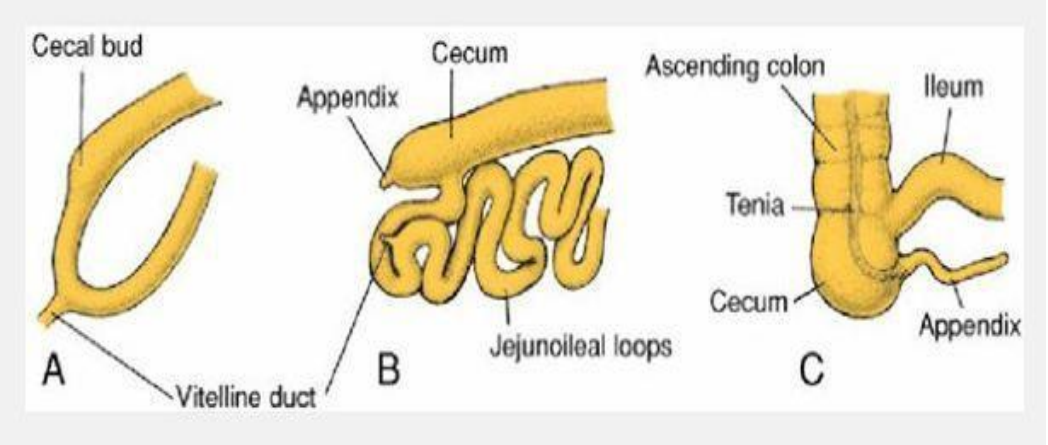


Figure 1: Successive stages in development of the caecum and appendix.

A. 7 weeks. B. 8 weeks. C. Newborn.

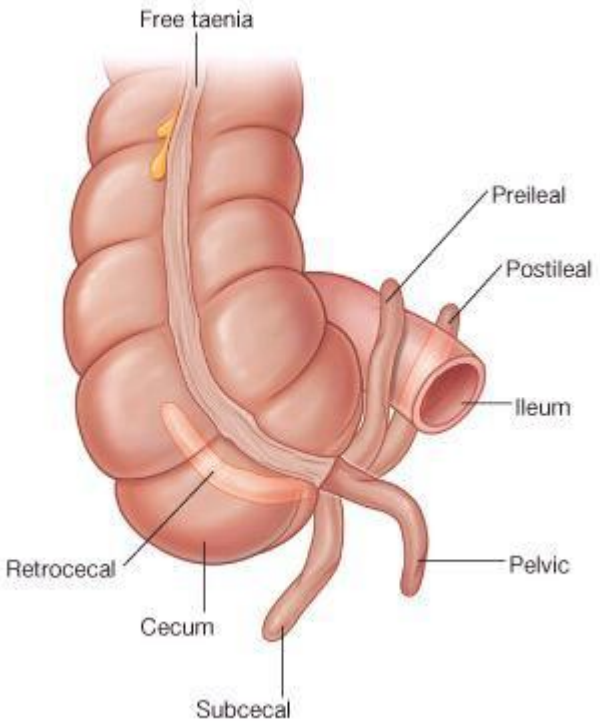


Figure 2. Various positions of appendix

4. Congenital diverticulum / appendicular band:

Unlike the acquired one, in this muscular layer is present.Vitelointestinal duct provides origin for some of the diverticulae and caecum may be developed from the the junction of these two structures. In this cases the diverticulum has fibrous band connection with the umbilicus.

Other than the band, a ring may be found extends upto the umbilicus known as appendiculo ovarian ligament.

ANATOMY OF VERMIFORM APPENDIX[32]

1. The appendicular situated on the posteromedial aspect of the caecum 2 cm below the ileocaecal orifice.

2. The appendicular orifice is occasionally guarded by an indistinct semilunar fold of mucous membrane, known as *'valve ofGerlacti.*

3. The orifice is marked on the surface by a point situated 2 cm below the junction of the trans-tubercular and right lateral planes

4. McBurney's point is the site of maximum tenderness in appendicitis. The point lies at the junction of lateral one-third and medial two-thirds of the line joining the right anterior superior iliac spine to the umbilicus.

It may occupy one of several positions.

1. The appendix may pass upwards and to the right. This is the paracolic or 11 O'clock position.

2. It may lie behind the caecum or colon, known as retrocaecal or 12 O'clock position. This is the commonest position of the appendix, about 65%.

3. The appendix may pass upwards and to the left. It points towards the spleen. This is the splenic or 2 O'clock position. The appendix may lie in front of the ileum (preileal) or behind the ileum (postileal).

4. It may pass horizontally to the left (as if pointing to the sacral promontory called promontoric or 3 O'clock position

5. It may descend into the pelvis called pelvic or 4 O'clock position. This is the second most common position about 30%.

6. It may lie below the caecum (subcaecal) and may point towards the inguinal ligament called as midinguinal or 6 O'clock position.

Lumen of Appendix

It is quite small and may be partially or completely obliterated after mid-adult lifeThe lumen of appendix is very narrow. There are *no villi.* The epithelium invaginates to form crypts of Lieberkuhn. Muscularis mucosae is ill defined.

Submucosa reveals many lymphoid masses. That is why it is called the *abdominal tonsil. Muscularis externa* comprises two layers. Outermost is the serous layer,

Peritoneal Relations

The appendix is suspended by a small, triangular fold of peritoneum, called the mesoappendix, or appendicular mesentery. The fold passes upwards behind the ileum, and is attached to the left layer of the mesentery. Occasionally, the mesoappendix may remain short of the apex.

Blood Supply

The appendicular artery is a branch of the lower division of the ileocolic artery. It runs behind the terminal part of the ileum and enters the mesoappendix at a short distance from its base. Here it gives a recurrent branch which anastomoses with a branch of the posterior caecal artery. The main artery runs towards the tip of the appendix lying at first near to and then in the free border of the mesoappendix. The terminal part of the artery lies actually on the wall of the appendix. Blood from the appendix is drained by the appendicular, ileocolic and superior mesenteric veins, to the portal vein...

NERVE SUPPLY:

Sympathetic nerves are derived from thoracic nine and ten segments through the coeliac plexus. Parasympathetic nerves are derived from the vagus. Referred pain of appendix is felt at umbilicus, similar to that of small intestine and testis.

Lymphatic Drainage

Most of the lymphatics pass directly to the ileocolic nodes, but a few of them pass indirectly through the appendicular nodes situated in the mesoappendix

Mesoappendix

The mesentery of the appendix is a triangular fold of peritoneum around the vermiform appendix. It is attached to the posterior surface of the lower end of the mesentery of the small intestine close to the ileocaecal junction. It usually reaches the tip of the appendix but some times fails to reach the distal third, in which case a vestigial low peritoneal ridge containing fat is present over the distal third. It encloses the blood vessels, nerves and lymph vessels of the vermiform appendix, and usually contains a lymph node.

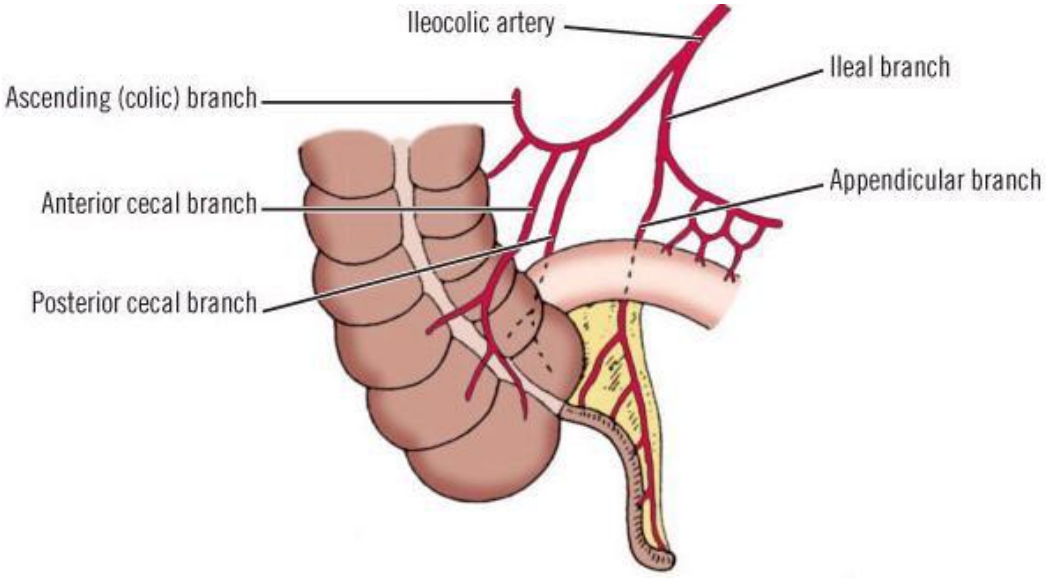


Figure 3. Blood supply of appendix

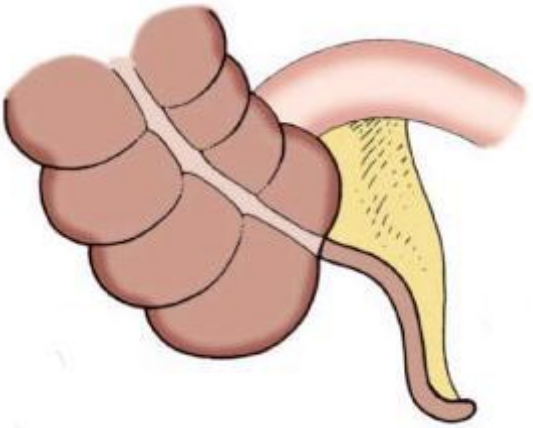


Figure 4. Mesoappendix

Caecal recesses

Several folds of peritoneum may exist around the caecum and form recesses. Paracaecal recesses are common sites for abscess formation following acute appendicitis.

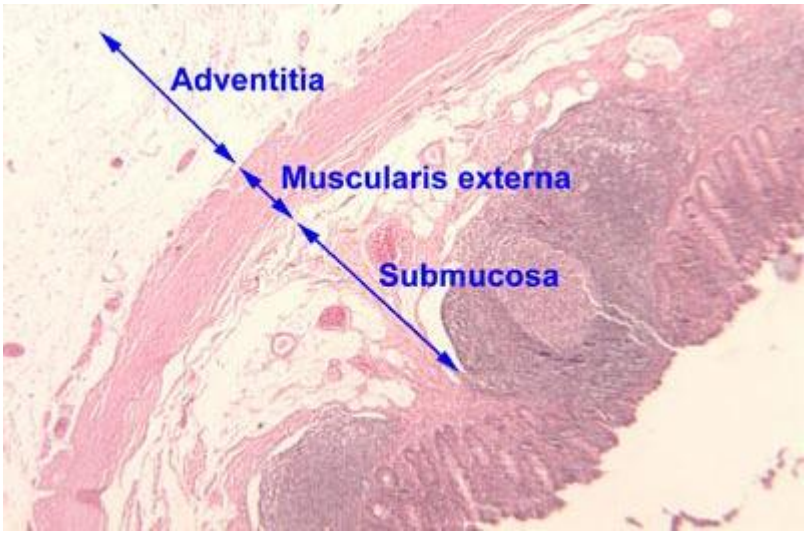
Others include, Superior ileocaecal recess, Inferior ileocaecal recess and Retrocaecal recess.

surface marking appendicular base- between the lateral and middle thirds of the straight line from the right ASIS to the umbilicus (**Mc Burney's point**),. The taenia coli converge and end on the base of the appendix.

Microstructure :

Histologically, appendix has four layers in its wall—

mucosa, *submucosa, muscularis* and *serosa*. The mucosa has patchy distribution of crypts and the submucosa has abundant lymphoid tissue. Argentaffin and nonargentaffin endocrine cells are present in the base of mucosal glands just as in the small intestine. The muscularis of the appendix has two layers (inner circular andouter longitudinal) as elsewhere in the alimentary tract.



FUNCTIONS OF THE APPENDIX

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Postulated functions of the appendix[32]:

1. Exocrine: There have been suggestions that the appendix in human has an exocrine function, assisting in digestion of plant foods. However the 2 ml of clear fluid secreted containing mucin, amylase and proteolytic enzymes per day in low concentrations cannot have any effect on food stuffs in the

caecum and food stuffs wouldn‟t ideally enter the appendix for processing.

2. Endocrine: The neuroendocrine cells and their secretory products in the appendix have not shown to have any selective endocrine functions.

3. Neuromuscular: It has been suggested that, the appendix may be the pacemaker for synchronized contraction and emptying that side of the bowel.

4. Lymphoid: The amount of the lymphoid tissue in the appendix is equal to that in the ascending, transverse and descending colon. There is a relative increases in IgM, IgA and IgG containing lymphocytes in the lamina propria of the appendix.

Stowens claims that the appendix is not a vestigial organ but has the same function as the thymus and possible function as a mammalian equivalent of the bursa of fabricus has been suggested.

Epidemiology of Appendicitis

Acute appendicitis is the most common general surgical emergency, and early surgical intervention improves outcomes. About 8% of people in Western countries have appendicitis at some time during their lifetime.[3]

The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately seven percent of all people undergoing appendicectomy for acute appendicitis during their lifetime. Over the 10 year period from 1987 to 1997, the overall appendicectomy rate decreased in parallel with a decrease in incidental appendicectomy.[33,34] However, the rate of appendicectomy for appendicitis has remained constant at 10 per 10,000 patients per year.[35] Despite the increased use of ultrasonography, computed tomography (CT) and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15.3%) and the rate of appendicular rupture. The percentage of misdiagnosed cases of appendicitis is significantly higher among women than among men (22.2 vs. 9.3%). The negative appendicectomy rate for women of

reproductive age is 23.2%, with the highest rates in women aged 40 to 49 years. The highest negative appendicectomy rate is reported for women >80 years of age.[34,35]

In the United States, 250,000 cases of appendicitis are reported annually, representing one million patient-days of admission. The incidence of acute appendicitis has been declining steadily since the late 1940s, and the current annual incidence is 10 cases per 100,000 population. Appendicitis occurs in seven percent of the US population, with an incidence of 1.1 cases per 1000 people per year. Some familial predisposition exists.

In Asian and African countries, the incidence of acute appendicitis is probably lower because of the dietary habits of the inhabitants of these geographic areas. The incidence of appendicitis is lower in cultures with a higher intake of dietary fiber. Dietary fiber is thought to decrease the viscosity of feces, decrease bowel transit time, and less formation of faecaliths, which predispose individuals to obstructions of the appendicular lumen.

In the last few years, a decrease in frequency of appendicitis has also been reported in Western countries, which may be related to changes in dietary fiber intake. In fact, the higher incidence of appendicitis is believed to be related to poor fiber intake in such countries.

AETIOLOGY[36]

The etiological factors still remain unknown and obscure although appendicitis is a common disease.

It is or has been, universally rare prior to the adoption of western standards of living. The riddle of appendicitis, its actual causes and its meteoric rise from an insignificant disease to the most common serious intra-abdominal inflammatory affection of western civilized areas-has been a matter of much speculation. It is rare in rural communities in economically less developed countries and its incidence is rising with economic development, migration to urban area and emigration to western countries. No individual with an appendix seems immune from the risk of developing appendicitis, but many contributory factors may be responsible.

1. **Age and Sex**:

No age is immune from the risk of developing appendicitis, which has been reported in new born (Shinaberger JH-1957) and also at the extremes of age. It is rare under the age of four year and after the age of 50 yrs. About 65% of the patients are under the age of 30 yrs and only 2% are 60 yrs and above. The incidence of appendicitis is maximum between 20 to 30yrs[3].

In teenagers and young adults - there is a slight male preponderance of 3:2. While in adults, the incidence of appendicitis is approximately 1.4 times greater in men than in women.

2. **Familial susceptibility**:

There are instances of appendicitis occurring in families, suggesting an inherited susceptibility. Downs (1942) operated 16 cases out of 22 closely related individuals for appendicitis. In each case appendix was sharply kinked at the base by a fibrous band, binding it to the lateral aspect of the

caecum. Males and females in direct inheritance shared the anomaly equally.

3. **Seasonal factors**:

There is, particularly in children, a possible association between seasonal respiratory tract infection and acute appendicitis. The lymphoid tissue in the appendix and tonsils may be simultaneously affected. A blood born origin of such cases may be supported by observation of such cases.

4. **Race and Diet**:

In general, appendicitis is associated with non- roughage diet and with the consumption of a high proportion of meat. Racial distribution may be related to diet, as many of those races said to escape appendicitis may develop the disease of civilization. The national distribution of the disease is interesting. It is common in highly industrialized countries, such as Great Britain, United States, France and Germany. In Denmark and Sweden it is low. In Spain, Greece, Italy and the rural parts of Rumania it is very low. Mc Carrison[37] states that during the early years of his practice in North -

West India, he never saw a case of appendicitis, but we find that in Indians it is not uncommon.

5. **Faecaliths**:

Non-calcified inspissated faecal masses are a common finding in a large proportion of appendices removed for acute disease. Ulceration or perforation usually occurs at or near a faecaliths may turn diffuse inflammatory lesion into gangrene.

6. **Constipation and Purgation**:

Constant and frequent use of purgation for constipations leads to violent peristaltic action, which results, favours and determines the perforation of inflamed appendix.

7. **Parasites**:

Blackadder (1824) reported a case in which a man died suddenly after a very severe bout of pain in the abdomen and who was found at autopsy to have a round worm impacted at the appendicaecal junction. Other parasites like thread worm injure mucus membrane or at times cause obstruction of the lumen of the appendix and cause acute inflammation of the appendix.

8. **Bacterial factors**:

The bacterial population of the normal appendix is similar to that of the normal colon. The appendicular flora remains constant throughout life with the exception of *Porphyromonas gingivalis.* This bacterium is seen only in adults.[40] The bacteria cultured in cases of appendicitis are therefore similar to those seen in other colonic infections such as diverticulitis. The principal organisms seen in the normal appendix, in acute appendicitis, and in perforated appendicitis are *Escherichia coli* and

Bacteroides fragilis.[38-41] However, a wide variety of both facultative and anaerobic bacteria and mycobacteria may be present (Table 1). Appendicitis is a polymicrobial infection, with some series reporting the culture of up to 14 different organisms in patients with perforation[38].

Aerobic and Facultative	Anaerobic
Gram-negative **bacilli** *Escherichia* *coli Pseudomonas* *aeruginosa Klebsiella*	**Gram-negative** **bacilli** Other *Bacteroide*s species *Bacteroides fragilis*
Gram-positive cocci *Streptococcus anginosus*	**Gram-positive cocci** *Peptostreptococcus* species
Other *Streptococcu*s species *Enterococcus* species	**Gram-positive bacilli** *Clostridium* species

Table 1. Common Organisms seen in Patients with Acute appendicitis

9. **Bands and Adhesions**:

Various abnormal peritoneal attachments of congenital origin have been described and if these cause kinking of the appendix, it results into obstruction. Inflammatory or acquired adhesions due to repeated attacks of appendicitis may induce final acute obstructive picture.

10. **Strangulation within a hernial Sac**:

Strangulation or trauma of the appendix, which lies in an internal or external hernial sac, may induce progressive changes similar to strangulated small bowel. Diffuse inflammation of an appendix in hernial sac may be aggravated by the obstructive effect at the neck of the sac. Amyand removed the first gangrenous appendix from the inguinal hernia[2]. Chatter (1966) removed the inflamed appendix from the femoral hernial sac.

11. **Trauma**:

This is a very rare cause of acute appendicitis, if the attack of acute appendicitis follows within 24 hrs after a blunt injury to right iliac region the probable cause of appendicitis is due to the displacement of faecaliths by trauma to the abdomen i.e. to the right iliac region and causing sudden obstruction. Birrel (1928) described four cases of this type, while Black (1948) reported 2 cases and Bhaje Kar (1953) 1 case[42].

12. **Acute appendicitis secondary to metastatic carcinoma**:

Kenneth (1966)[43] reviewed total 13 cases from the literature, of these 7 cases have presented as acute appendicitis and in 5 of them, the cases showed appendicular perforation at operation. In 5 cases, breast was the site of primary Ca. Metastatic carcinoma of the appendix due to the encroachment of the growth presents as acute obstructive appendicitis leading to perforation and other complications.

13. Epidemic Form:

Acute appendicitis may occur as an epidemic and the portal of entry for the infection is the nasopharynx and the organisms are usually streptococci.

14. **Amoebic appendicitis**:

De S. N., and Sengupta[44] reported a case of acute appendicitis due to amoebic infection.

15. **Vascular factors**:

The appendicular artery is an end artery. It is possible that extramural ischemia may play a role in this disorder. Any thing that compromises the external blood supply could therefore contribute to ischemia, inflammation and hence secondary infection in the appendix.

Pathogenesis[23]

Obstruction of the lumen is the dominant etiologic factor in acute appendicitis. Faecaliths are the most common cause of appendicular obstruction. Less common causes are hypertrophy of lymphoid tissue, inspissated barium from previous x-ray studies, tumours, vegetable and fruit seeds, and intestinal parasites. The frequency of obstruction rises with the severity of the inflammatory process. Faecaliths are found in 40% of cases of simple acute appendicitis, in 65% of cases of gangrenous appendicitis without rupture, and in nearly 90% of cases of gangrenous appendicitis with rupture.

Traditionally the belief has been that there is a predictable sequence of events leading to eventual appendicular rupture. The proximal obstruction of the appendicular lumen produces a closed-loop obstruction, and continuing normal secretion by the appendicular mucosa rapidly produces distension. The luminal capacity of the normal appendix is only 0.1 mL. Secretion of as little as 0.5 mL of fluid distal to an obstruction raises the intraluminal pressure to 60 cm H_2O. Distension of the appendix stimulates the nerve endings of visceral afferent stretch fibres, producing vague, dull, diffuse pain in the mid abdomen or lower epigastrium. Peristalsis also is stimulated by the sudden distension, so that some cramping may be superimposed on the visceral pain early in the course of appendicitis. Distension increases from continued mucosal secretion and from rapid multiplication of the resident bacteria of the appendix. Distension of this magnitude usually causes reflex nausea and vomiting, and the diffuse visceral pain becomes more severe. As pressure in the organ increases, venous pressure is exceeded. Capillaries and venules are occluded, but arteriolar inflow continues, resulting in engorgement and vascular congestion.

The inflammatory process soon involves the serosa of the appendix and in turn parietal peritoneum in the region, which produces the characteristic shift in pain to the right lower quadrant.

The mucosa of the GI tract, including the appendix, is susceptible to impairment of blood supply; thus its integrity is compromised early in the process, which allows bacterial invasion. As progressive distension encroaches on, first the venous return and subsequently the arteriolar inflow, the area with the poorest blood supply suffers most: ellipsoidal infarcts develop in the antimesenteric border. As distension, bacterial invasion, compromise of vascular

supply, and infarction progress, perforation occurs, usually through one of the infarcted areas on the antimesenteric border. Perforation generally occurs just beyond the point of obstruction rather than at the tip because of the effect of diameter on intraluminal tension.

This sequence is not inevitable, however, and some episodes of acute appendicitis apparently subside spontaneously. Many patients who are found to have acute appendicitis at operation give a history of previous similar, but less severe, attacks of right lower quadrant pain. Pathological examination of the appendices removed from these

patients often reveals thickening and scarring, suggesting old, healed acute inflammation.[36,45]

The strong association between delay in presentation and appendicular perforation supported the proposition that appendicular perforation is the advanced stage of acute appendicitis; however, recent epidemiologic studies have suggested that non perforated and perforated appendicitis may, in fact, be different diseases.[45]

Pathology[23]

Morphology

Appendicular inflammation is associated with obstruction in 50% to 80% of cases, usually in the form of a faecalith and, less commonly, a gallstone, tumor, or ball of worms (oxyuriasis vermicularis).

Continued secretion of mucinous fluid in the obstructed viscus presumably leads to a progressive increase in intraluminal

pressure sufficient to cause eventual collapse of the draining veins. Ischemic injury then favors bacterial proliferation with additional inflammatory edema and exudation, further embarrassing the blood supply. Nevertheless, a significant minority of inflamed appendices have no demonstrable luminal obstruction, and the pathogenesis of the inflammation remains unknown.

At the earliest stages, only a scanty neutrophilic exudate may be found throughout the mucosa, submucosa, and muscularis propria. Subserosal vessels are congested, and often there is a modest perivascular neutrophilic infiltrate. The inflammatory reaction transforms the normal glistening serosa into a dull, granular, red membrane; this transformation signifies early acute appendicitis for the operating surgeon. At a later stage, a prominent neutrophilic exudate generates a fibrinopurulent reaction over the serosa.

As the inflammatory process worsens, there is abscess formation within the wall, along with ulcerations and foci of

suppurative necrosis in the mucosa. This state constitutes acute suppurative appendicitis.

Further vascular compromise leads to large areas of hemorrhagic green ulceration of the mucosa and green-black gangrenous necrosis through the wall, extending to the serosa, creating acute gangrenous appendicitis, which is quickly followed by rupture and suppurative peritonitis.

The histological criterion for the diagnosis of acute appendicitis is neutrophilic infiltration of the muscularis propria. Usually, neutrophils and ulcerations are also present within the mucosa. Since drainage of an exudate into the appendix from alimentary tract infection may also induce a mucosal neutrophilic infiltrate, evidence of muscular wall inflammation is requisite for the diagnosis.

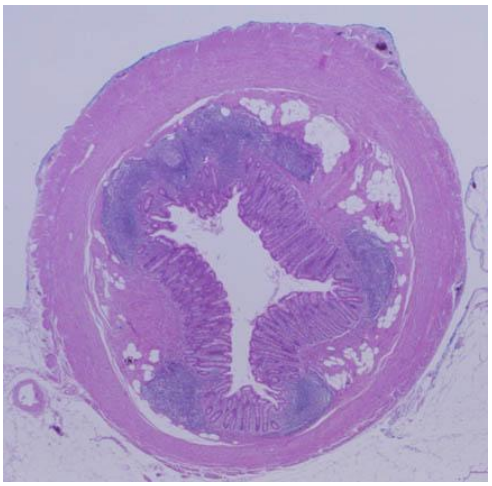

Figure 5: Normal histology of axppendicitis

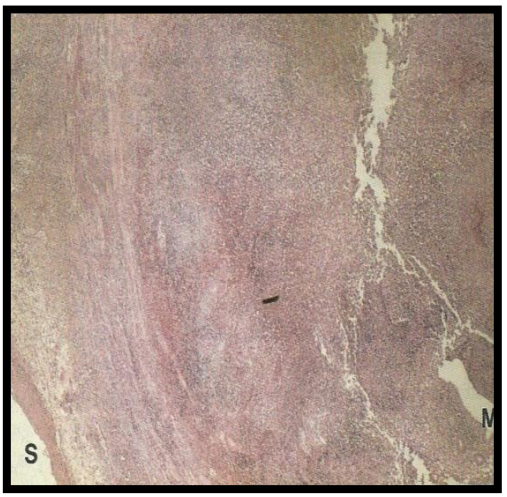

Figure 6. Histology of inflamed appendicitis

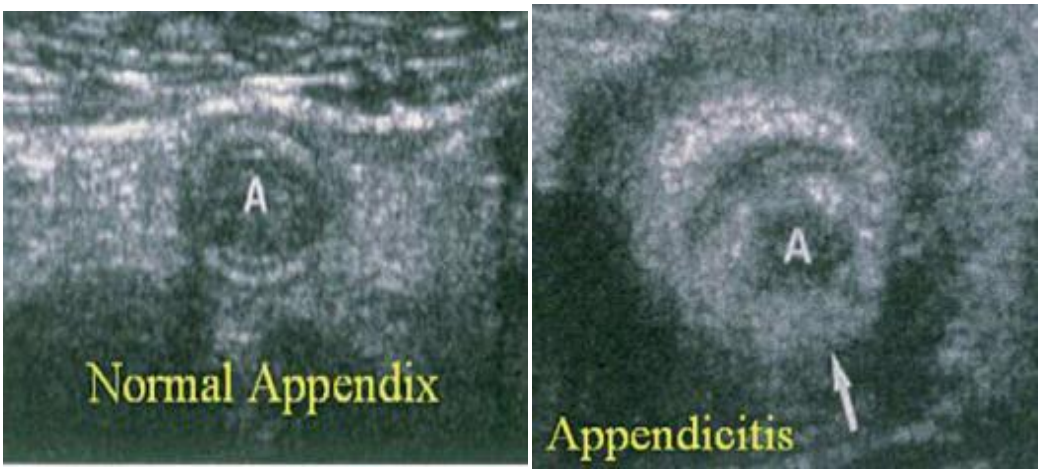

Figure 7. USG finding of a normal appendix and inflammed appendix

DIAGNOSIS

History[1]

The classical features of acute appendicitis begin with poorly localised colicky abdominal pain. This is due to mid-gut visceral discomfort in response to appendicular inflammation and obstruction. The pain is frequently, first, noticed in the peri-umbilical region and is similar to, but less intense than, the colic of small bowel obstruction. Central abdominal pain is associated with anorexia, nausea and usually one or two episodes of vomiting that follow the onset of pain (Murphy‟ s triad). Most common clinical feature is anorexia. The patient often gives a history of similar discomfort that settled spontaneously. A family history is also useful as up to one-third of children with appendicitis have a first-degree relative with a similar history.

Visceral pain starts around the umbilicus due to distension of appendix, later after few hours, somatic pain occurs in right iliac fossa due to irritation of parietal peritoneum due to infl a med appendix.

Pain eventually becomes severe and diffuse which signifies spread of infection into the general peritoneal cavity.

Vomiting*:* Due to reflex pylorospasm. _

*Constipatio*n is the usual feature but diarrhoea can occur if appendix is in postileal or pelvic positions. Fever, tachycardia, foetor oris are other features. Urinary frequency*:* Infl amed appendix may come in contact with bladder and can cause bladder irritation.

Tenderness and rebound tenderness at *McBurney's point* in right iliac fossa *(release sign—Blumberg's sign)* are typical.

Rovsing's sign: On pressing left iliac fossa, pain occurs in right iliac fossa which is due to shift of bowel loops which irritates the parietal peritoneum.

Because appendicitis is so common, a high index of suspicion for appendicitis is warranted in all patients with abdominal pain.[46]

Physical examination[1]

The diagnosis of appendicitis made usually by the clinical examinations rather than the lab investigations or history.

The charecteristic features low-grade fever, localised RIF tenderness, guarding and rebound tenderness. On Inspection,there may be decreased abdominal movements during respiration.

On palpation, from the left iliac fossa moving towards the right iliac fossa,one can able to feel muscle guarding in the McBurney‟ s point. Asking the patient to cough or gentle percussion over the site of maximum tenderness will elicit rebound tenderness. Cutaneous hyperaesthesia may be demonstrable in the right iliac fossa, but is rarely of diagnostic value.

Multiple signs can be detected on physical examination to contribute to the diagnosis of appendicitis.

1. ***Mc Burney's sign:*** Maximum tenderness at Mc Burney‟ s point.
2. ***Blumberg's sign:*** A hand kept in the right iliac fossa is progressively pressed with each movement of expiration. It is then removed suddenly; the patient will wince or cry with pain, if the sign is positive, this indicates inflammation of

the parietal peritoneum. It is useful sign in the absence of guarding or rigidity.

3. ***The pointing sign:*** The patient have to locate the site of origin of pain and its spread

4. ***Rovsing's sign:*** This sign is positive as a result of pressure on the left side of the colon, forcing the gas into the caecum distending the caecum and surrounding of the inflamed focus resulting in pain.

5. ***Psoas sign:*** Pain with flexion of the leg at the right hip, can be seen with a retrocecal appendix due to inflammation adjacent to the psoas muscle.

6. ***The Cope's(obturator) sign:*** Pain with rotating the flexed right thigh internally, indicates inflammation adjacent to the obturator muscle in the pelvis.

7. ***Sherren's sign:*** Sherren in 1925, pointed out this Sherren's triangle and is defined as the triangle bounded by lines joining umbilicus, right anterior superior iliac spine and pubic symphysis. Hyperesthesia is elicited by gently striking the skin.

It is compared with left side. If hyperesthesia is present it indicates the perforation of the appendix. This sign is although classic, it is not reliable. It depends upon the discrimination capacity of the patient.

8. ***Baldwin's test for retrocaecal appendix****:* After identifying the tender spot in the right flank, light pressure is maintained over the spot and the patient is asked to lift the right lower limb keeping the knee in straight position. This produces increased pain in the loin and the patient drops the leg with pain. This is a positive sign of retrocaecal appendicitis. Sometimes there may be irritation of the ureters with pain shooting around flank. Sometimes red blood corpuscle may be found in the urine.

9. ***Shifting Tenderness (Alder's):*** The most tender spot is marked first, the patient is put in left lateral position and point of maximum tenderness is marked again. If the tender spot shifts probably it is not a case of appendicitis. This sign is useful to differentiate appendicitis from mesenteric lymphadenitis and painful uterine conditions in pregnancy.

Rectal examination[2]:

Digital per rectal examination should be done in all cases of acute abdomen. Tenderness on right side is significant. As digital examination itself produces discomfort, by palpating left lateral and posterior wall of rectum is compared with that produced on right side. It may be the only positive sign in pelvic appendicitis. It is positive in one-third cases; perfect examination can also detect a pelvic abscess.

Investigations

The diagnosis is usually clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 30% of cases. The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly.[1]

A number of Laboratory and Imaging studies have been devised to assist diagnosis.

Laboratory Tests

There is no gold standard test for appendicitis but it may be helpful in arriving the diagnosis.

WBC

A White Blood Cell count (WBC)may have significant role with leucocytosis, with more than 75% neutrophils.

A completely normal leukocyte count and differential count is found in about 10% of patients with acute appendicitis. A high white blood cell count (>20,000/mL) suggests complicated appendicitis with either gangrene or perforation.[3]

In early cases WBC count may be normal.There may be raise in WBC count over the time.

C-reactive protein

C-reactive protein (CRP) is an acute-phase reactant synthesized by the liver in response to infection or inflammation and rapidly increases within the first 12 hours. CRP has been reported to be useful in the diagnosis of appendicitis; however, it lacks

specificity and cannot be used to distinguish between sites of infection. CRP levels of greater than 1 mg/dl are commonly reported in patients with appendicitis, but very high levels of CRP in patients with appendicitis indicate gangrenous evolution of the disease, especially if it is associated with leukocytosis and neutrophilia.

However, CRP normalization is known to occur 12 hours after onset of symptoms. Several prospective studies have shown that in adults who have had symptoms for longer than 24 hours, a normal CRP level has a negative predictive value of 97-100% for appendicitis.[47-49]

Multiple studies have been done evaluating the sensitivity of CRP level alone for the diagnosis of appendicitis in patients selected to undergo appendicectomy. Gurleyik et al noted a CRP sensitivity of 96.6% in 87 of 90 patients with histologically proven disease.[50]

Imaging Studies

The various imaging techniques for diagnosis include plain Xray, USG and CT scan..

Plain radiographs

Plain X-ray may show lumbar scoliosis towards right due to psoas spasm which is not uncommon; faecolith on the right side; obliteration of preperitoneal fat line due to retrocaecal appendicitis; segmental ileus in caecum and terminal ileum; speckled extraluminal gas in right iliac fossa, gas in appendix, pneumoperitoneum (very rare); intestinal obstruction (occasionally only); soft tissue mass in mass or abscess of appendix—all these features are very much nonspecifi c. X-ray is useful to rule out DU perforation, intestinal obstruction, ureteric stone.

Radio-opaque appendix in a plain X-ray. It could be calcified or have calcified content.

Ultrasonography (USG)

Sonographic criterias for appendicitis (85% Specifi city)

Noncompressible appendix of size > 6 mm AP diameter,

hyperechoic thickened appendix wall > 2 mm—*target sign*.

Appendicolith.

Interruption of submucosal continuity.

Periappendicular fluid.

Ultrasonography has the advantages of being a non-invasive modality requiring no patient preparation that also avoids exposure to ionizing radiation. For these reasons, it is commonly used in children and in pregnant women with doubtful diagnosis.

Pelvic ultrasound can be especially useful in excluding pelvic pathology, such as tubo-ovarian abscess or ovarian torsion, which may mimic acute appendicitis.[42]

Computed tomography

Computed tomography (CT) is commonly used in the evaluation of adult patients with suspected acute appendicitis, especially so in the elderly.[3] CT has a high sensitivity and specificity in the diagnosis of appendicitis,[52] and rule out other causes of abdominal pain that mimic appendicitis.

Improved imaging techniques, including the use of 5-mm sections, have resulted in increased accuracy of CT scanning,[53] which has a sensitivity of about
90% and a specificity of 80% to 90% for the diagnosis of acute appendicitis among patients with abdominal pain.

Controversy remains as to the importance of intravenous, oral gastrointestinal, and rectal contrast in improving diagnostic accuracy.

In general, CT findings of appendicitis increase with the severity of the disease. Classic findings include a distended appendix greater than seven mm in diameter and circumferential wall thickening, which may give the appearance of a halo or target. As inflammation progresses, one may see periappendicular fat stranding,

edema, peritoneal fluid, phlegmon, or a periappendicular abscess. CT detects appendicoliths in about 50% of patients with appendicitis and also in a small percentage of people without appendicitis. Among patients with abdominal pain, the positive predictive value of the finding of an appendicolith on CT remains high at about 75%.

Laproscopy

Although most patients with appendicitis will be accurately diagnosed based on history, physical exam, laboratory studies, and if necessary, imaging techniques, there are a small number in whom the diagnosis remains elusive. For these patients, diagnostic laparoscopy can provide both a direct examination of the appendix and a survey of the abdominal cavity for other possible causes of pain.

Laparoscopy can serve as both a diagnostic and therapeutic maneuver for patients with acute abdominal pain and suspected acute appendicitis.

Laparoscopy is probably most useful in the evaluation of females with lower abdominal complaints, because appendicectomy is performed on a normal appendix in as many as 30 to 40% of these patients. Differentiating acute gynecologic pathology from acute appendicitis can be effectively accomplished using the laparoscope.[23]

Barium enema studies

In the past, barium enema examination was used to diagnose appendicitis. However in the era of ultrasonography and CT scanning, barium enema study has absolutely no role in the diagnosis of acute appendicitis.

Scoring Systems

A number of clinical and laboratory-based scoring systems have been devised to assist diagnosis. The most widely used is the Alvarado score. A score of seven or more is strongly predictive of acute appendicitis.[1]

Features	Score
Symptoms	
□ Migratory RIF pain	1
□ Anorexia	1
□ Nausea and vomiting	1
Signs	
□ Tenderness (RIF)	2
□ Rebound tenderness	1
□ Elevated temperature	1
Laboratory	
□ Leucocytosis	2
□ Shift to left	1

Table 2: The Alvarado score

Liver Function Tests

Importance of hyperbilirubinemia or elevated Serum Bilirubin (serum bilirubin) and its association in acute appendicitis has being postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acute appenditics and its complications such as appendicular perforation.[55]

BILIRUBIN METABOLISM

Destruction of senescent RBC in the RE system 80-85%

Marrow destruction of matured RBC (15-20%)

Heme containing protein (liver turnover)- minimal

Hemoglobin

Heme oxygenase

Biliverdin

Biliverdin reductase

Bilirubin

binds with albumin

Bilirubin albumin complex transported to the liver

Liver takes up bilirubin

UDP Glucuronyl transferase

Conjugate with glucuronic acid and forms

monoglucuronide and diglucuronide

After deconjugation, bilirubin is absorbed at terminal

ilium, ileocecal junction

Free bilirubin

Reduction

Urobilinogen 20% (gives urine color) and

Stercobilinogen 80% (gives stool color)

Oxidized and re-entered into enterohepatic circulation (13%)

Excreted through urine (4-7%)

Bilirubin is produced from the destruction of senescent RBC's by the removal of the iron by the action of the enzyme heme oxygenase; the reaction liberates carbon monoxide, the only reaction in the body releasing carbon monoxide. The intermediate product being biliverdin. Bilirubin a water insoluble compound is transported

to the liver bound to albumin.

In the liver the bilirubin is taken up activity by two mechanisms. The first being a membrane bound carrier protein and the second being by two cytoplasmic proteins namely protein Y and Z. These proteins pick up the bilirubin diffusing into the cytoplasm.

Once in the hepatocyte the bilirubin is bound to glucuronic acid thus forming bilirubin mono and diglucuronide by the enzyme UDP glucuronyl transferase. The enzyme reduced products get excreted as stercobilinogen.

The kidneys excrete a part of the absorbed bilirubin as urobilinogen and the rest enters the enterohepatic circulation.

Hyperbilirubinemia and appendicitis

Hyperbilirubinemia, has not been considered as a potential marker for preoperative diagnosis of acute appendicitis and appendicular perforation until now.Increased secretion and decreased bilirubin clearance has a role in the hyperbilirubinemia of patients with appendicular perforation.

Bacterial infections cause hepatic dysfunction leading to abnormalities in bile acid production and bile flow. This results in hyperbilirubinemia.

Extrahepatic bacterial infection, as in perforated appendicitis, have a proinflammatory cytokine and nitric oxide – triggered cholestasis by affecting hepatocellular and bile duct function.[60]

Most common bacterial species causing acute appendicitis are *Escherichia coli* and *Bacteroides fragilis.* These organisms interfere with hepatocyte microcirculation and cause sinusoidal damage .

E. Coli endotoxin leads to impaired bile production.And also, *E. Coli* infection causes hemolysis of erythrocytes. This leads to hyperbilirubinemia.

Acute Appendicitis/Appendicular perforation (Inflammatory response causes appendix to become more oedematous and ischmeic)

↓

Causes transmigration/translocation of bacteria/toxins/cytokines

↓

Leading to endotoxemia / bacteremia

↓

Invasion of Bacteria into the hepatic parenchyma interferes with the physiology of excretion of bile

↓

Hyperbilirubinemia

Cholestasis in severe bacterial infection, particularly in childhood or post operatively, is presumably hepatocellular in nature. It can also be related to cholestatic effect of endotoxin on sodium-potassium-ATPase.[57]

All the constituents of bile show an increased level in serum. Conjugation of biliary substance is intact but excretion is defective. Serum alkaline phosphatase is raised. The rise is due to increased synthesis or release of enzymes from liver or biliary plasma membrane.

The minimal hepatocellular damage may be suspected by noting minimal elevated transaminase value and sometimes serum bilirubin.

There are no sufficient number of studies involving large number of patients to ascertain relationship between hyperbilirubinemia and acute appendicitis.

Literature review

It is postulated that there is relationship between hyperbilirubinemia and acute appendicitis and its complications.

A retrospective analysis by Sand M et al, done at The Department of General and Visceral Surgery, Augusta Krankenanstalt, Academic Teaching Hospital of the Ruhr University, Bochum, Germany involving 538 patients (306 females: 232 males, mean age, 35.6 years) with histologically confirmed acute appendicitis who underwent conventional or laparoscopic appendicectomy between January 2004 to December 2007 found the mean bilirubin level of all patients was 0.9mg/dl (±0.6 SD mg/dl; range 0.1 to 4.3mg/dl; median 0.7mg/dl).

Patients with Appendicular perforation, however had a mean bilirubin level of 1.5mg/dl (±0.9 SD mg/dl; range 0.4 to 4.3 mg/dl; median 1.4mg/dl), which was significantly higher than those with a non perforated appendicitis *($p<0.05$)*. The Specificity of hyperbilirubinemia for appendicular perforation was 0.86 compared with 0.55 for white blood count and 0.96 for C-reactive protein.[69] The study concluded that the Patients with hyperbilirubinemia and clinical symptoms of appendicitis should be identified as having probability of appendicular perforation than those with normal bilirubin levels.[68]

A retrospective analysis done at Department of Surgery, St. Luke's Hospital, Kilkenny, Ireland by Emmanuel A et al, whereby retrospective analysis of appendicectomies performed in two hospitals (n=472) was done. Data collected included laboratory and histological results. Patients were grouped according to histology findings and comparisons were made between the groups.[69] They found that the mean bilirubin levels were higher for patients with simple appendicitis compared to those with a non-inflamed appendix ($p<0.001$). More patients with simple

appendicitis had hyperbilirubinemia on admission (30% vs 12%) and the odds of these patients having appendicitis were over three times higher (odds ratio: 3.25, $p<0.001$). Hyperbilirubinemia had a specificity of 88% and a positive predictive value of 91% for acute appendicitis. Patients with appendicitis who had a perforated or gangrenous appendix had higher mean bilirubin levels ($p=0.01$) and were more likely to have hyperbilirubinemia ($p<0.001$). The specificity of hyperbilirubinemia for perforation or gangrene was 70%. The specificities of white cell count and C-reactive protein were less than hyperbilirubinemia for simple appendicitis (60% and 72%) and perforated or gangrenous appendicitis (19% and 36%). The authors concluded that hyperbilirubinemia is a valuable marker for acute appendicitis. Patients with hyperbilirubinemia are also more likely to have appendicular perforation or gangrene. Bilirubin should be included in the assessment of patients with suspected appendicitis.[69]

A retrospective review done at the Department of Surgery, Keck School of Medicine of the University of Southern California and Los Angeles County, USC Medical Center, Los Angeles, CA, USA between January 2005 to December 2005 by Estrada J et al studied the relationship between hyperbilirubinemia and appendicitis. Patients with liver function tests on admission and pathologically confirmed appendicitis were included in the study. Age, duration of symptoms, temperature, white blood cell counts, systemic inflammatory response score, and bilirubin levels were independent variables in a logistic regression analysis assessing factors predicting the presence or absence of appendicular gangrene/perforation.[56] Elevated total bilirubin levels (>1mg/dl) were found in 59(38%) of 157 patients. Patients with gangrene/perforation were significantly *(p=0.004)* more likely to have hyperbilirubinemia than those with acute suppurative appendicitis. No statistical differences were observed for any of the other variables. On logistic regression the only significant relationship between the presence or absence of appendicular gangrene and perforation was the presence of hyperbilirubinemia

(p=0.031, 95% confidence interval 1.11–7.6). The odds of appendicular perforation are three times higher (odds ratio 2.96) for patients with hyperbilirubinemia compared to those with normal bilirubin levels. Hyperbilirubinemia is frequently associated with appendicitis. Elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.[54]

MATERIALS AND METHODS

The study was conducted in the Department of General Surgery, Govt.Stanley Medical College,Chennai during the period of November 2013 to November 2014.

Study design

A prospective non randomised study.

Source

The present study was conducted in the Department of Surgery, Govt.Stanley Medical College,Chennai

Study period

One year from November 2013 to November 2014..

Source of data

Patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under the Department of Surgery, Govt.stanley medical college,chennai during the study period.

Sample size

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation were studied.

Sampling method

The sample size was calculated based on the following formula.

$$n = \frac{Z^2 \times p \times q}{d^2}$$

Where,

n = Sample size

Z = 1.96 ≈ 2 (considering confidence as 95%)

p = prevalence (prevalence is taken as 50% as exact prevalence is not known)

q = 100 – p that is, 50%

d = Absolute error which was 10%

Selection criteria

Inclusion

- All patients diagnosed as acute appendicitis clinically on admission.
- All patients diagnosed as appendicular perforation clinically on admission.

- For both these groups, only patients with histopathological report suggestive of acute appendicitis or appendicular perforation were included.

Exclusion

- All patients documented to have a past history of-
  - Jaundice or Liver disease.
  - Chronic alcoholism (that is intake of alcohol of > 40 g/day for Men and > 20 g/day in Women for 10 years).[71]
  - Hemolytic disease.
  - Acquired or congenital biliary disease.
- All patients with positive HBsAg.
- All patients with cholelithiasis.
- All patients with cancer of hepato-biliary system.

Procedure

Ethical clearance has been obtained from "Ethical Clearance Committee" of the institution for the study. Based on the selection criteria patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under Department of Surgery, Govt.stanley medical college,chennai during the study period were screened. The nature of the study was explained to the patients. And

the patients were included in this study after getting written informed consent. History and clinical examination was done for all and recorded in the profoma

The following tests were carried out on admission.

- Routine blood investigations (Complete blood count, platelet count, reticulocyte count).
- Peripheral smear to rule out hemolytic anemia.
- Serum haptoglobulin if peripheral smear and blood tests indicate features of hemolytic anemia.
- Serum Bilirubin (Total and Direct bilirubin).
- Liver Function Tests (LFTs) which include;
    - SGPT (Alanine transaminase).
    - SGOT (Aspartate transaminase).
    - ALP (Alkaline phosphatase).
- Seropositivity for HbsAg
- Urine analysis (routine and microscopy).

The serum bilirubin and LFTs were carried out using the Auto Analyser machine available in the hospital and HbsAg was tested by ELISA / Spot technique using HEPALISA© or HEPACARD© kit.

Reference Range of Serum Bilirubin and Liver Enzymes[23]

Test	Normal Range
Serum Bilirubin	
Total	0.3 - 1.0 mg/dl
Direct	0.1 – 0.3 mg/dl
Liver Enzymes	
SGPT	0 – 35 U/L
SGOT	0 – 35U/L
ALP	30 – 120U/L

The results were grouped as Normal or Raised (hyperbilirubinemia) as per the above reference values.

Statistical analysis

The data obtained was tabulated on Microsoft excel spreadsheet and analysed as below.

- Patients with clinical diagnosis of acute appendicitis having hyperbilirubinemia were expressed in percentage as

$$= \frac{\text{Patients with clinical diagnosis of acute appendicitis with elevated Serum bilirubin level}}{\text{All patients with clinical diagnosis of acute appendicitis}}$$

- Mean of the level of elevation of Serum bilirubin was calculated for patients with clinical diagnosis of acute appendicitis.

- Patients with clinical diagnosis of appendicular perforation having hyperbilirubinemia were expressed in percentage as;

$$= \frac{\text{Patients with clinical diagnosis of appendicular perforation with elevated Serum bilirubin}}{\text{All patients with clinical diagnosis of appendicular perforation}}$$

- Mean of the level of elevation of serum bilirubin were calculated for patients with clinical diagnosis of appendicular perforation.

- A hypothesis was made based on the observation of the level of the two means.

- Also, sensitivity, specificity, positive predictive value, negative predictive value and Odds ratio was determined by 2 x 2 table as below.

	Acute appendicitis	Appendicular perforation
Raised Sr. Bilirubin	A	B
Normal Sr. Bilirubin	C	D
	a + c	b + d

Sensitivity: $\frac{a}{a + c} \times 100$

Specificity: $\frac{d}{b + d} \times 100$

Positive predictive value : $\frac{a}{a + b} \times 100$

Negative predictive value: $\frac{d}{c + d} \times 100$

Odds ratio: $\frac{ad}{bc}$

RESULTS

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation admitted in the Department of General surgery, Govt.stanley medical college,chennai were studied.

As per the study, the age group 11-20years is most commonly affected (44%) followed by age group 21-30 (32%). The youngest patients of this study were of 8 years old while the oldest patient was a 70 year lady

Table 3: Distribution of patients by age

Age Group (years)						
≤10	11-20	21-30	31-40	41-50	51-60	61-70
8	44	32	8	3	4	1

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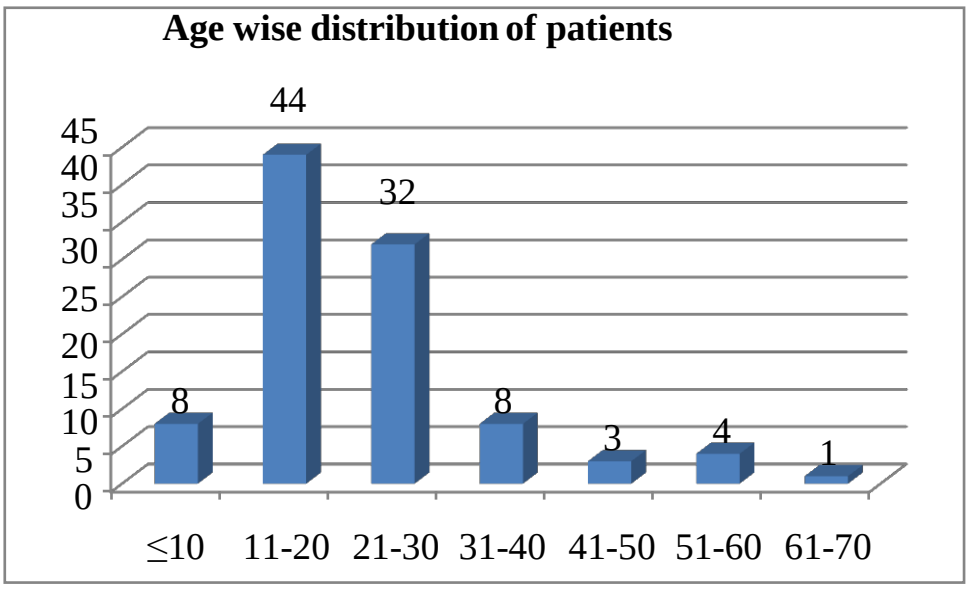

Age wise distribution of patients
45
40
35
30
25
20
15
10
5
0
44
32
8
8
3
4
1
≤10
11-20
21-30
31-40
41-50
51-60
61-70

Table 4: Sex distribution

Sex	Number	Percentage
Male	56	56
Female	44	44
Total	**100**	**100.00**

Out of 100 patients enrolled for the study, 56 patients (56%) were males while the remaining 44 patients (44%) were females.

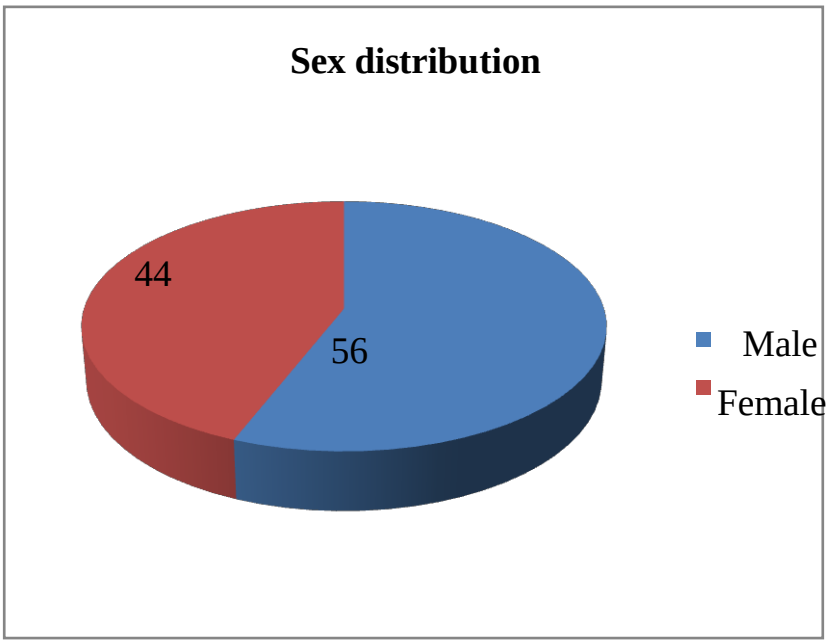


Table 5: Mean Age distribution among sex

Sex	Age (yrs)	SD
Male	24	11.93
Female	21.9	11.93
Overall	**23.1**	**11.99**

The overall mean age of all 100 patients was 23.1 ± 11.99 years (range, 11.11–35.09 years). The average age in males and females was 24 ± 11.93 years (range, 12.07 –35.93 years) and 23.1 ± 11.93 years (range, 11.17 –35.03 years) respectively.

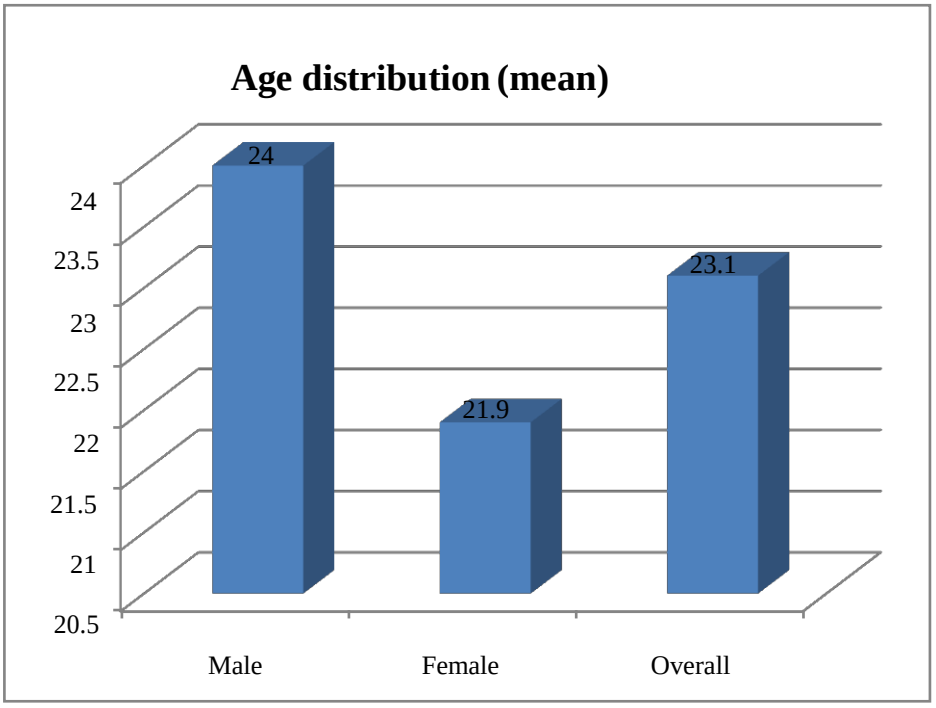


Table 6: Liver Function Tests

Parameters	Mean	SD
Total bilirubin (mg/dL)	1.5	0.8
Direct bilirubin (mg/dL)	1.0	0.7
Indirect bilirubin (mg/dL)	0.5	0.2
SGOT (U/L)	27.9	12.2
SGPT (U/L)	25.9	11.0
ALP (U/L)	80.8	21.6

The mean Total bilirubin of all 100 patients was 1.5 ± 0.8 mg/dL (range, 0.7 – 2.3 mg/dL) while the Direct bilirubin was 1.0 ± 0.7 mg/dL (range, 0.3-1.7 mg/dL). The mean SGOT and SGPT were 27.9 ± 12.2 U/L (range, 15.7-40.1 U/L) and 25.9 ± 11.0 U/L (range, 14.9 – 35.9 U/L). The mean ALP values were 80.8 ± 21.6 U/L (range, 59.2 -102.4 U/L).

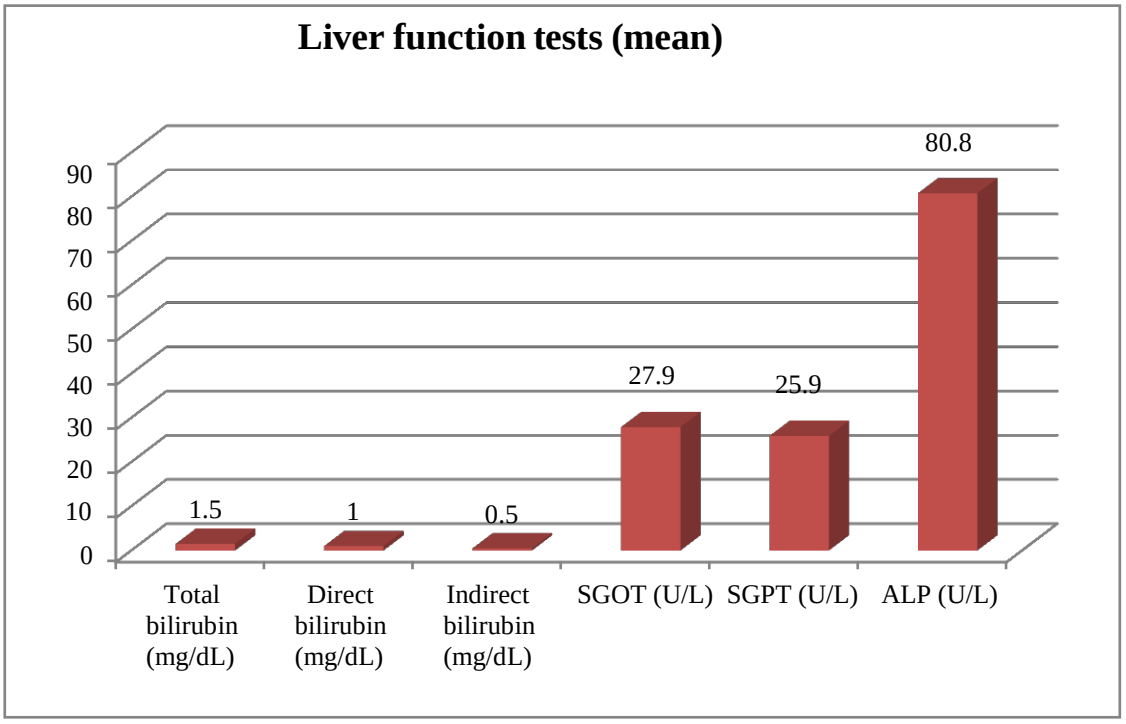

Liver function tests (mean)
90
80
70
60
50
40
30
20
10
0
1.5
1
0.5
27.9
25.9
80.8
Total bilirubin (mg/dL)
Direct bilirubin (mg/dL)
Indirect bilirubin (mg/dL)
SGOT (U/L)
SGPT (U/L)
ALP (U/L)

Table 7: Total bilirubin levels

Total bilirubin (mg/dL)	Number	Percentage
< 1.0	26	26.0
≥ 1.0	74	74.0
Total	**100**	**100.00**

26 patients (26%) of all 100 patients were found to have normal bilirubin levels (≤ 1.0 mg/dL), while 74 patients (74%) had raised bilirubin levels (> 1.0 mg/dL).

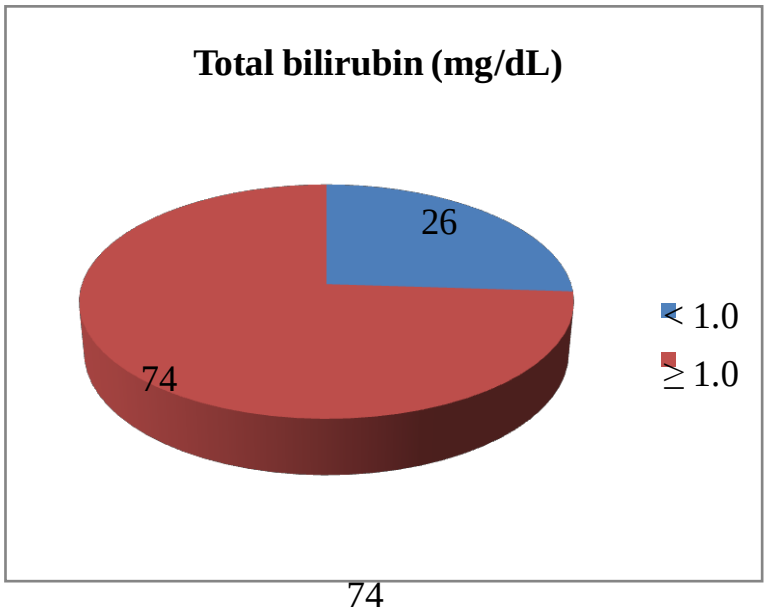


Table 8: Bilirubin levels in patients with uncomplicated acute appendicitis as diagnosis

Total bilirubin (mg/dL)	Distribution in Patients with uncomplicated Acute Appendicitis	
	Number	Percentage
> 1.0	58	71.60
≤ 1.0	23	28.40
Total	**81**	**100.00**

Of 81 patients diagnosed as uncomplicated acute appendicitis, 58 patients (71.6%) had raised bilirubin levels (> 1.0 mg/dL), while the remaining 23 patients (28.4%) had normal levels (≤ 1.0 mg/dL).

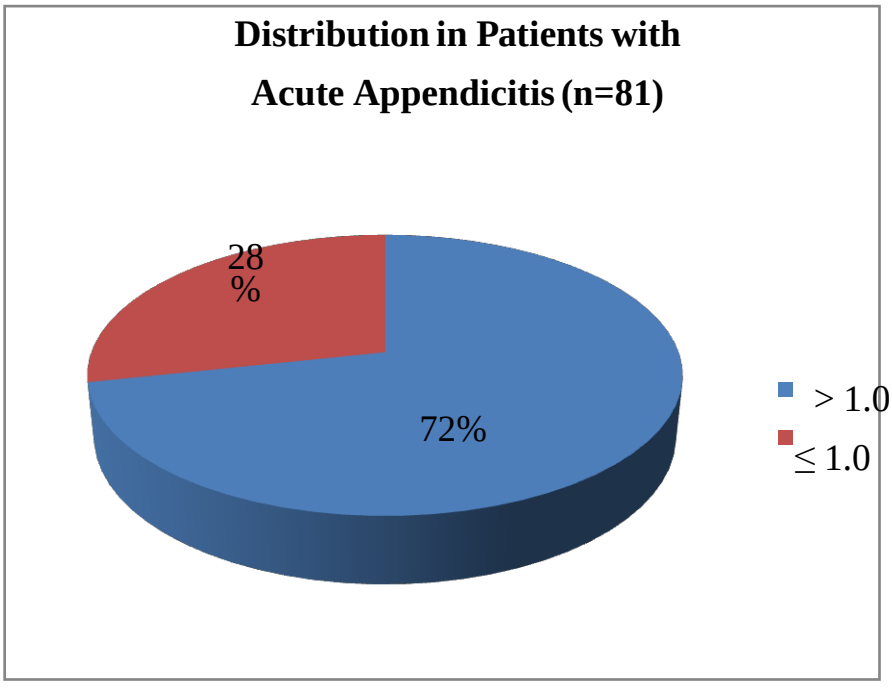


Table 9. Bilirubin levels in patients with Appendicular perforation diagnosis

Total bilirubin (mg/dL)	Distribution in Patients with Appendicular perforation	
	Number	Percentage
> 1.0	16	84.21
< 1.0	03	15.79
Total	**19**	**100.00**

19 patients diagnosed as Appendicular perforation, 16 patients (84.21%) had raised bilirubin levels (> 1.0 mg/dL), while the remaining 03 patients (15.79%) had normal levels (≤ 1.0 mg/dL).

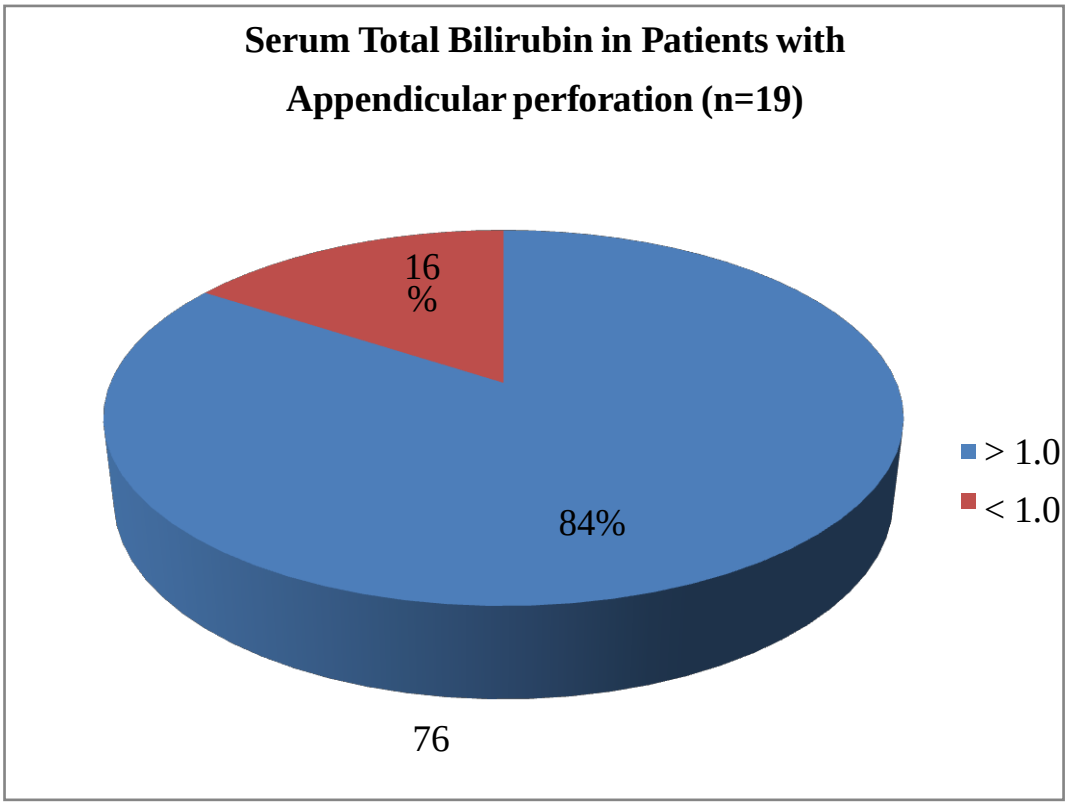


Table 10. Total leukocyte count (TLC)

TLC count (/mm^3)	Distribution (n=100)	
	Number	Percentage
≤ 11,000	65	65
> 11,000	35	35
Total	**100**	**100.00**

65 patients (65%) had Total Leukocyte count less than 11,000/mm^3 while 35 patients (35%) counts above 11,000/mm^3.

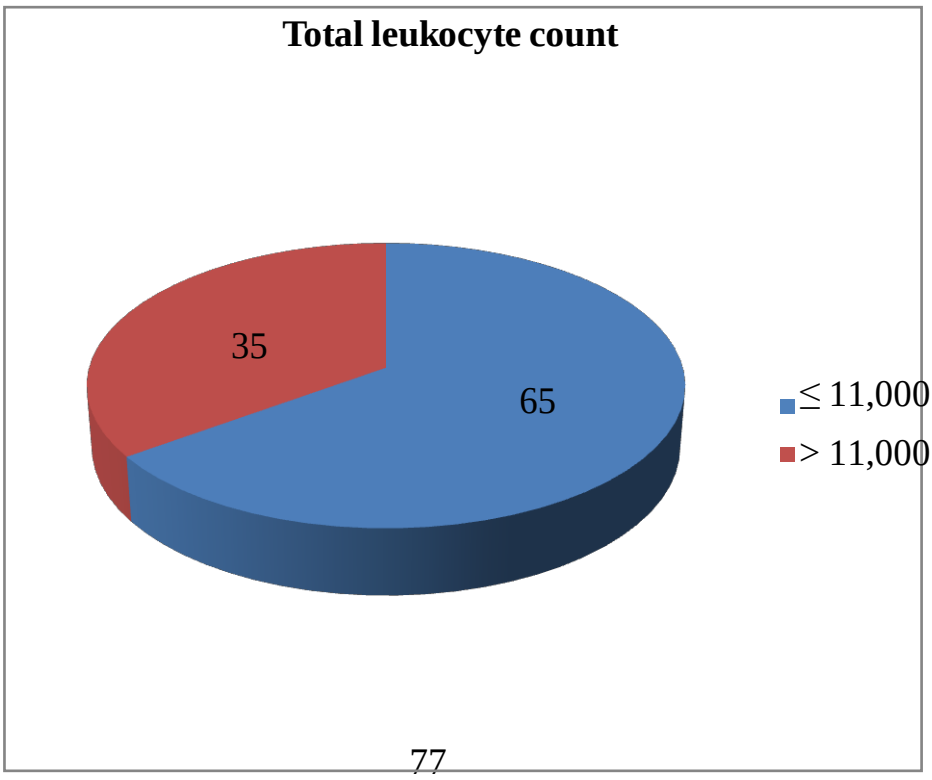
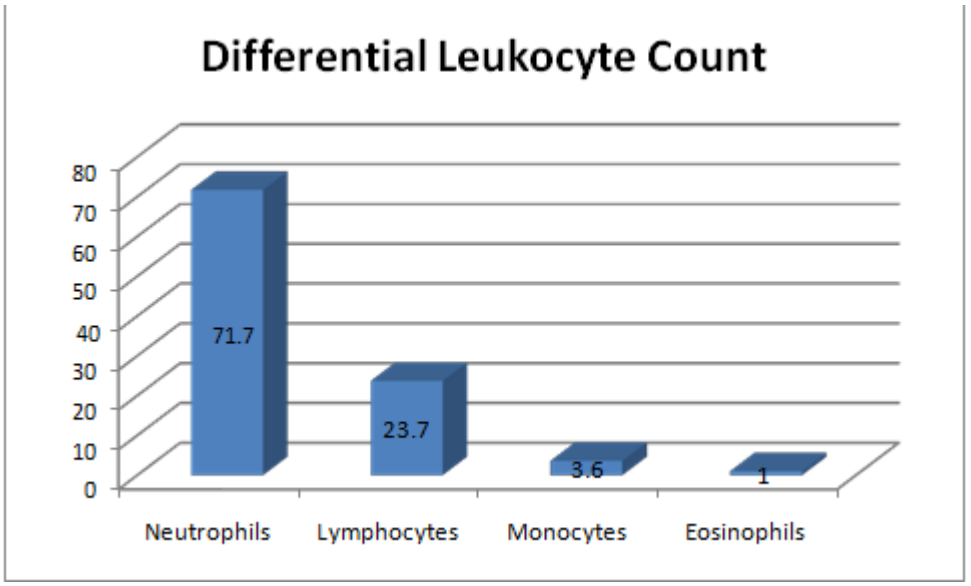


Table 11. Differential Leukocyte Count (DLC)

Differential Leukocyte Count (DLC		Mean value	
		Mean	SD
Total count (/mm^3)		10030	3712
Differential count	Neutrophils	71.7	11.5
	Lymphocytes	23.7	10.7
	Monocytes	3.6	2.6
	Eosinophils	1.0	1.4

The mean of TLC count in all patients was 10030±3712/mm^3 (range, 6318 - 13742/mm^3), in which the highest percentage constituted neutrophils with 71.7% followed by 23.7% by Lymphocytes.



Differential Leukocyte Count

Table 12. Pre-Operative Diagnosis

Pre – Operative Diagnosis	Distribution (n=100)	
	Number	Percentage
Acute appendicitis	91	91
Appendicular perforation	09	09
Total	**100**	**100**

In the study population of 100 patients, 91 patients (91%) were diagnosed as acute appendicitis while 9 patients (9%) were diagnosed with Appendicular perforation.

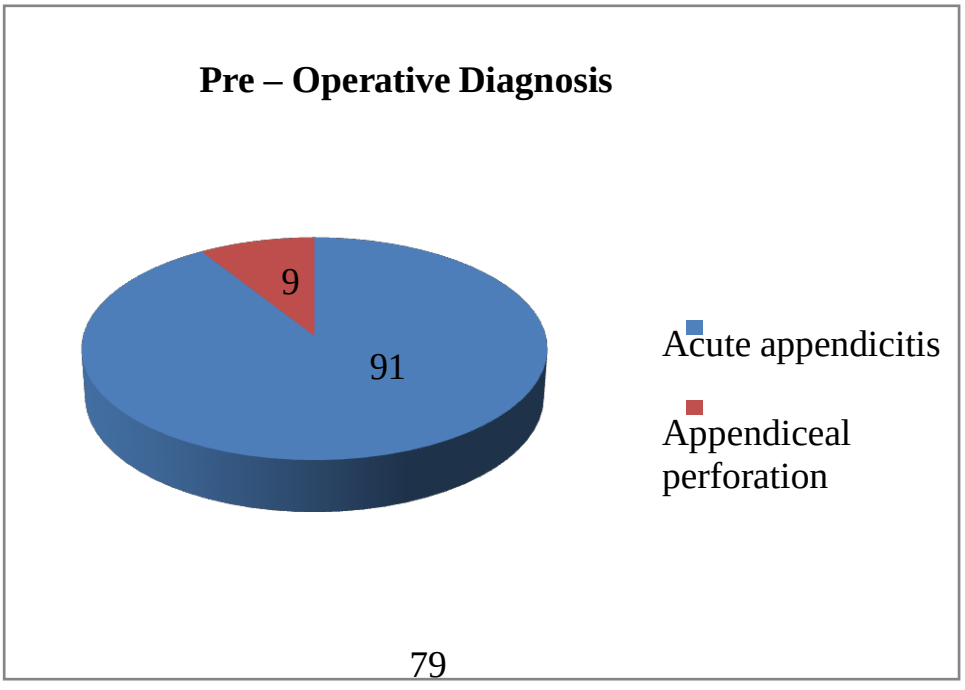


Table 13. Ultrasonographic findings

Findings	Distribution (n=100)	
	Number	Percentage
Normal	18	18
Acute Appendicitis	69	69
Appendicular perforation	13	13
Total	**100**	**100**

On Ultrasonography, 69 patients (69%) were diagnosed as Acute appendicitis, 13 patients (13%) as Appendicular perforation and 18 patients (18%) were reported as normal ultrasonographic findings.

Ultrasonographic findings

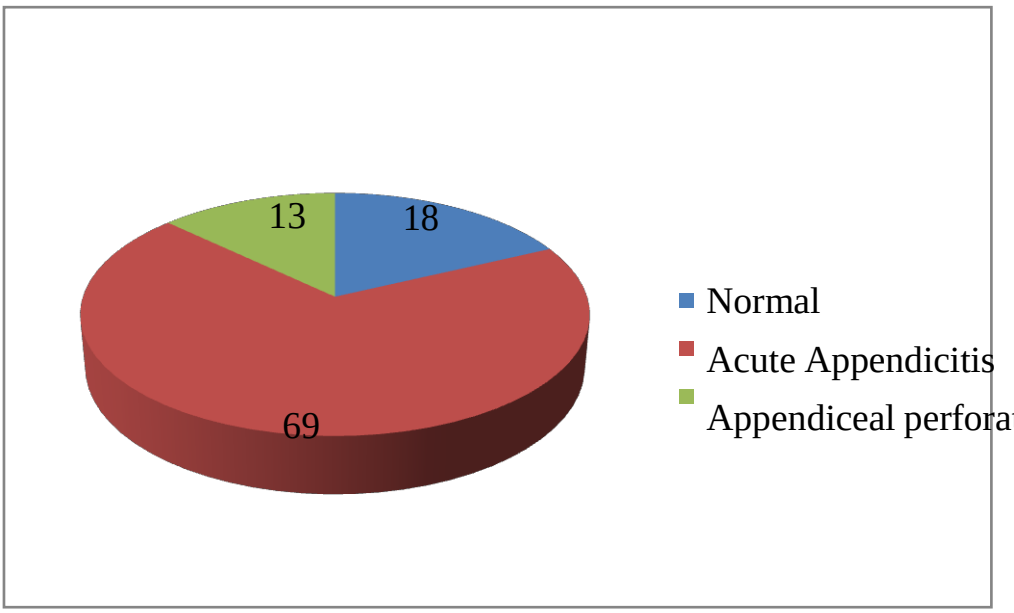


Table 14. Histopathological diagnosis

Diagnosis	Distribution (n=100)	
	Number	**Percentage**
Acute appendicitis	81	81
Appendicular perforation	19	19
Total	**100**	**100**

Histopathologically, 81 patients (81%) were confirmed as Acute appendicitis while 19 patients (19%) were diagnosed with Appendicular perforation.

Histopathological diagnosis

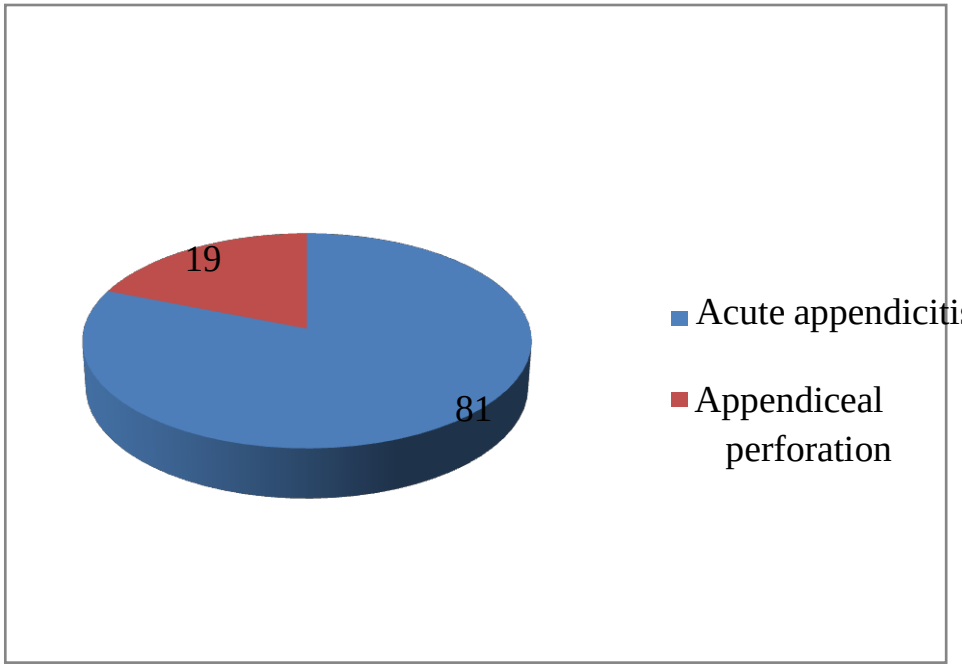


Table 15. Comparison of mean serum bilirubin levels in patients with acute appendicitis and Appendicular perforation

Bilirubin levels (mg/dL)	Diagnosis			
	Acute appendicitis		Appendicular perforation	
	Mean	SD	Mean	SD
Total bilirubin	1.4	0.65	1.9	1.16
Direct bilirubin	0.9	0.57	1.2	1.06
Indirect bilirubin	0.5	0.21	0.70	0.33

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.4 ±0.65 mg/dL (range, 0.75 – 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9±1.16 mg/dL (range, 0.74 – 3.06 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with Acute appendicitis were 0.9±0.57 mg/dL and 0.5±0.21 respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation were 1.2±1.06 mg/dL and 0.70±0.33 mg/dL respectively.

Figure 21: Mean Bilirubin values of Acute Appendicitis and Appendicular perforation

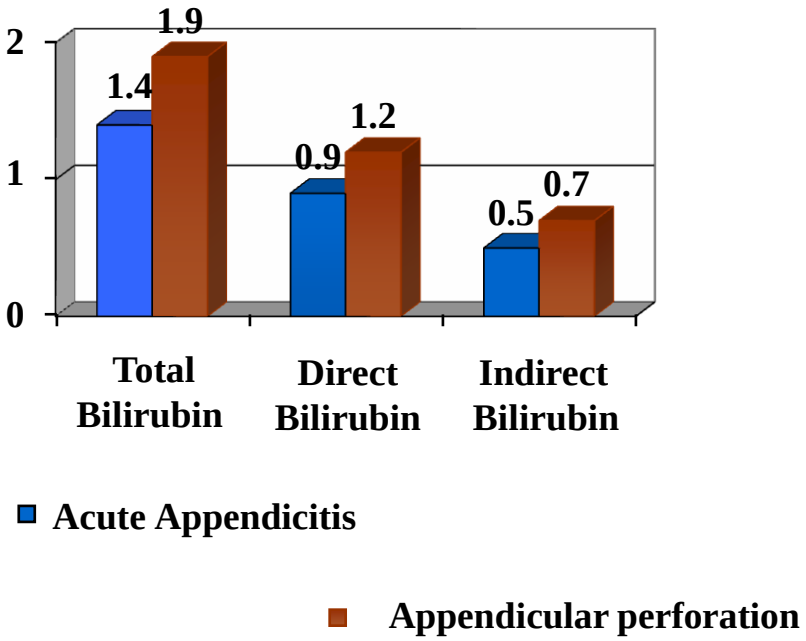


Table 16. Correlation of acute appendicitis and Appendicular perforation with total serum bilirubin levels

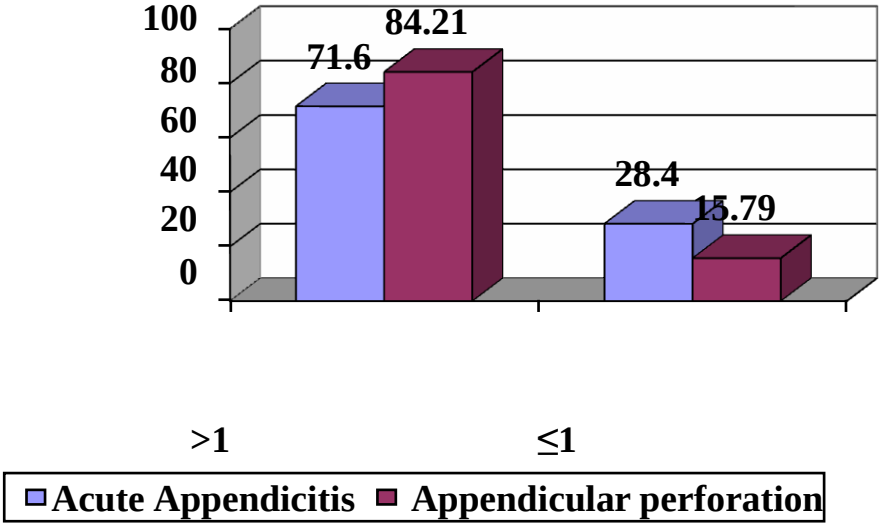
Serum bilirubin (mg/dL)	Final diagnosis (n=100)			
	Acute appendicitis (n=81		Appendicular perforation (n=19)	
	Number	%	Number	%
> 1.0	58	71.6	16	84.21
≤ 1.0	23	28.4	03	15.79
Total	**81**	**100.00**	**19**	**100.00**

58 patients (71.6%) of the total patients diagnosed with Acute appendicitis (n=81) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 23 patients (28.4%) had normal bilirubin levels (≤ 1.0 mg/dL). Similarly,

16 patients (84.21%) of the total patients diagnosed with Appendicular perforation (n=19) were found to have elevated bilirubin levels (> 1.0 mg/dL)

while 03 patients (15.79%) had normal bilirubin levels (≤ 1.0 mg/dL).

Figure 22: Bilirubin values among patients with Acute Appendicitis and Appendicular perforation



From Table, following values were calculated as -

Sensitivity

$$= \frac{a}{a + c} = \frac{58}{58 + 16} = 71.6\%$$

Therefore, sensitivity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 71.6%.

Specificity

$$= \frac{d}{b + d} = \frac{3}{16 + 3} = 15.79\%$$

Therefore, specificity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 15.79%

Positive predictive value

$$= \frac{a}{a + b} = \frac{58}{58 + 16} = 78.38\%$$

Therefore, Positive predictive value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 78.38%.

Negative predictive value

$$= \frac{d}{c + d} = \frac{3}{23 + 3} = 11.54\%$$

Therefore, Negative predictive value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 11.54%.

Odds ratio:

$$= \frac{ad}{bc} = \frac{58 \times 3}{23 \times 16} = 0.472$$

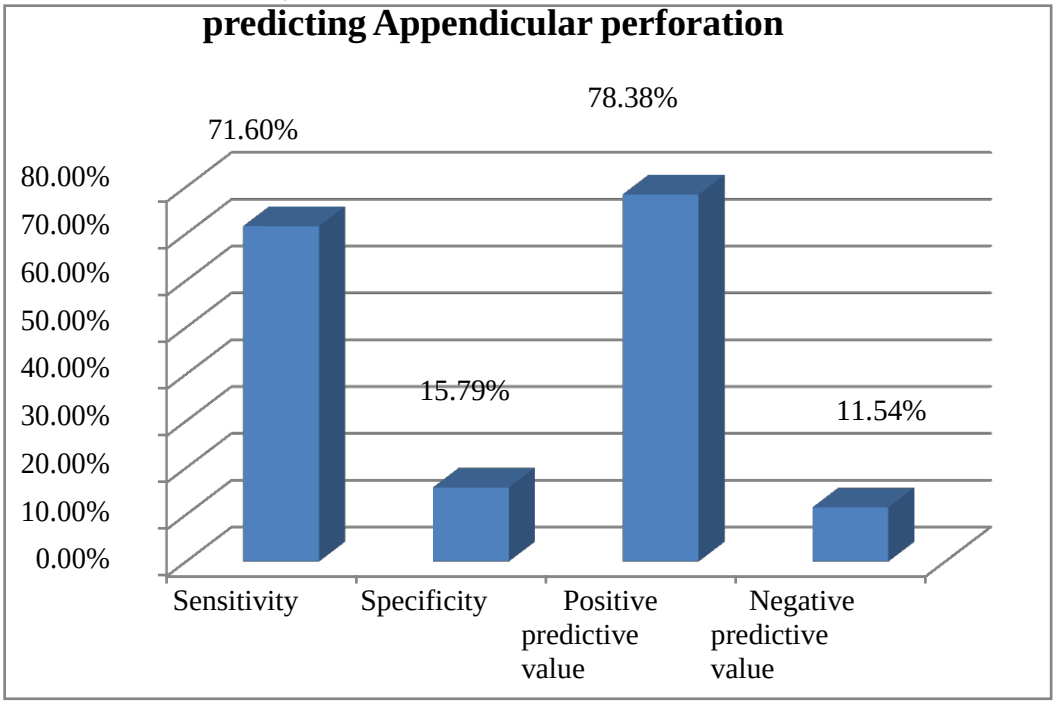
Therefore, Odds ratio is 0.472.

Table 17. Accuracy of serum bilirubin as a marker in predicting Appendicular perforation

	Accuracy
Sensitivity	71.6%
Specificity	15.79%
Positive predictive value	78.38%
Negative predictive value	11.54%
Odds ratio	0.472

The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and Appendicular perforation was 71.6% and 15.79% respectively. Similarly the Positive predicative value and Negative predicative value for the same is 78.38% and 11.54% respectively. The Odds r atio was calculated to be 0.472.

Accuracy of serum bilirubin as a marker in predicting Appendicular perforation



DISCUSSION

Acute appendicitis is the most common cause of " acute abdomen" in young adults. Appendicectomy is the most frequently performed emergency abdominal operation and is often the first major procedure performed by a surgeon in training.[1] About 8% of people in Western countries have appendicitis at some time in their lifetime.[3]

The peak incidence of acute appendicitis is in the second and third decade of life. It is relatively rare in infants, and becomes increasingly common in childhood and early adult life. The incidence of appendicitis is equal in males and females before puberty. In teenagers and young adults, the male – female ratio increases to 3:2 at age 25.[1] The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately 7% of all people undergoing appendectomy for acute appendicitis during their lifetime.[33,34]

Obstruction of the lumen is believed to be the major cause of acute appendicitis.[3] Faecoliths are the usual cause of obstruction. Less- common causes are hypertrophy of lymphoid tissue, tumors, intestinal parasites.[23] The bacteriology of normal appendix is similar to that of normal colon.

The principal organism seen in normal appendix, in acute appendicitis, and in perforated appendicitis are *Escherichia Coli* and *Bacteroids fragilis*. However a wide variety of both facultative and anaerobic bacteria may be present.[23]

The diagnosis of acute appendicitis is essentially clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 50% of cases.[4] The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly[1] as such procedures are associated with complications in 50% cases.[5] Hence, the diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations.

A new tool to help in the diagnosis of acute appendicitis would thus be welcome.

Serum Bilirubin level elevation will help in the accuracy of clinical diagnosis of acute appendicitis and more importantly help in foreseeing and preventing impeding complications of acute appendicitis.

This study was taken up with this thought – that is it possible to add serum bilirubin as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the credibility to help us foresee an impending complication of acute appendicitis?

Importance of hyperbilirubinemia and its association in acute appendicitis has being postulated recently. There are only a few case reports in the available literature that describe the finding of hyperbilirubinemia in patients of acute appendicitis.[54] It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications.[54]

The present study was undertaken to study the relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

This study was conducted in the Department of General Surgery, Govt.stanley medical college,chennai over a period of one

year from November 2013 to November 2014 on 100 patients with clinical diagnosis of Acute appendicitis and Appendicular perforation.

In the present study of the 100 patients enrolled for the study, 56 patients (56%) were males while the remaining 44 patients (44%) were females.The mean age in our study population (100 patients) was 23.1 ± 11.99 years (range, 11.11–35.09 years). This is consistent with the quoted incidence of Appendicitis in the literature where it is most frequently seen in patients in their second through fourth decades of life.[33,34] The average age group in males 24 ± 11.93 years (range, 12.07 –35.93 years) was slightly higher than females 23.1 ± 11.93 years (range, 11.17 –35.03 years).

Hyperbilirubinemia (> 1.0 mg/dL) in our study was found in 74 patients (74%) of all the 100 patients (n=100) enrolled in the study, while 26 patients (26%) had normal bilirubin levels (≤ 1.0 mg/dL). Estrada et al[54] had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean total serum bilirubin of all 100 patients was 1.5 ± 0.8 mg/dL (range, 0.7 – 2.3 mg/dL), which was above the normal range (≤ 1.0 mg/dL) considered for the study, hence indicating the occurrence

of hyperbilirubinemia. The mean of Direct bilirubin was 1.0 ± 0.7 mg/dL (range, 0.3-1.7 mg/dL) while that of Indirect bilirubin was 0.5±0.2 mg/dL (range, 0.3 – 0.7 mg/dL). Our finding was consistent with hyperbilirubinemia found in a study conducted by Khan S,[15] who found average level of serum bilirubin in his study population to be 2.38 mg/dL.

All patients were found to have SGOT and SGPT within the normal range, thus excluding any associated liver pathology (Exclusion criteria). The mean SGOT and SGPT were 27.9 ± 12.2 U/L (range, 15.7-40.1 U/L) and 25.9 ± 11.0 U/L (range, 14.9 – 35.9 U/L). The mean ALP values were 80.8 ± 21.6 U/L (range, 59.2 -102.4 U/L).

In our study population of 100 patients, 91 patients (91%) were diagnosed as acute appendicitis pre-operatively while 09 patients (9%) were diagnosed with Appendicular perforation.

The diagnosis was confirmed post-operatively by histopathological reports (HPR) and those differing from the pre-operative diagnosis were excluded from the study.

Amongst the patients diagnosed with Acute appendicitis without perforation (n=81), 58 patients (71.6%) were found to have elevated bilirubin (>1.0 mg/dL) while only 23 patients (28.4%) had normal bilirubin levels (≤1.0 mg/dL). In patients diagnosed with Appendicular perforation (n=19), 16 patients (84.21%) had bilirubin elevated (>1.0 mg/dL), while only 3 patients (15.79%) had normal levels (>1.0 mg/dL). Thus, Hyperbilirubinemia was found in most of the patients diagnosed with acute appendicitis (71.6%) or Appendicular perforation (84.21%).

The total leukocyte count was found elevated in just 35 patients (35%) of the total 100 patients. The mean of TLC count in all patients was 10030±3712/mm3 (range, 6318 - 13742/mm3), in which the highest percentage constituted Neutrophils with 71.7% followed by 23.7% by Lymphocytes.

On Ultrasonography, 69 patients (69%) were diagnosed as Acute appendicitis, 13 pateints (13%) as Appendicular perforation and 18 patients (18%) were reported as normal ultrasonographic findings. Ultrasonography per- se was 82% sensitive for appendicitis and/or Appendicular perforation, hence Ultrasonography is a helpful tool in diagnosing appendicitis or perforation.

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.4 ±0.65 mg/dL (range, 0.75 – 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9±1.16 mg/dL (range, 0.74 – 3.06 mg/dL). Hence, we see that patients with Appendicular perforation had higher levels of bilirubin as compared to that of acute appendicitis. So we infer that, patients with features suggestive of appendicitis with higher values of bilirubin, are more susceptible of having Appendicular perforation than those with normal or slightly elevated total serum bilirubin.

Sand et al[68] in his study found the mean bilirubin levels in patients with Appendicular perforation to be significantly higher than those with a non- perforated appendicitis.

The Direct bilirubin and indirect bilirubin in patients diagnosed with acute appendicitis were 0.9±0.57 mg/dL and 0.5±0.21 respectively. Similarly, direct bilirubin and indirect bilirubin in patients diagnosed with Appendicular perforation were 1.2±1.06 mg/dL and 0.70±0.33 mg/dL respectively.

The Sensitivity, Specificity, Positive predictive value, Negative predictive value and Odds ratio was calculated from a 2x2 table. Sensitivity and Specificity of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 71.6% and 15.79% respectively. Similarly Positive predictive value and Negative predicative value of bilirubin in predicting acute appendicitis and Appendicular perforation diagnosis was 78.38% and 11.54% respectively. The Odd‟ s ratio was calculated to be 0.472.

The sensitivity in our study was more than that by Sand et al[68] in which, he found the sensitivity and specificity in his study of hyperbilirubinemia for predicting Appendicular perforation to be 70% and 86.0% respectively.

CONCLUSION

The present study suggests-

- Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis remains essentially still - clinical. Its level come out to be a credible *aid* in diagnosis of acute appendicitis and would be helpful investigation in decision making.

- Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia higher than the normal range should be identified as having a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

SUMMARY

Acute appendicitis is the most common cause of "acute abdomen" in young adults. Diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. Importance of hyperbilirubinemia or elevated Serum Bilirubin and its association in acute appendicitis has been postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and its complications.

The present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

The present study was conducted in the Department of Surgery, Govt.stanley medical college,chennai during the period of November 2013 to November 2014. A total of 100 patients with clinical diagnosis of acute appendicitis or Appendicular perforation

were studied. The serum bilirubin and LFTs were carried out in all the patients.

In this study, males (56%) outnumbered females (44%) and overall the mean age was 23.1 ± 11.99 years. Mean total bilirubin was noted as 1.5 ± 0.8 mg/dL (range, 0.7 – 2.3 mg/dL) while direct bilirubin was 1.0 ± 0.7 mg/dL (0.2-

1.7 mg/dL). The mean SGOT and SGPT were 27.9 ± 12.2 U/L

(range, 15.7-40.1U/L) and 25.9 ± 11.0 U/L (range, 14.9 35.9U/L).

The mean ALP values were 80.8 ± 21.6 U/L (range, 59.2 -102.4 U/L).

Normal bilirubin values were seen in 26% patients while, 74% had raised bilirubin levels (Hyperbilirubinemia). Of 81 patients with acute appendicitis, 71.6% had raised bilirubin levels, while 28.4% had normal levels. 19 patients were diagnosed as Appendicular perforation, 16 patients (84.21%) had raised bilirubin levels, while the remaining 03 patients (15.79%) had normal levels. The total leukocyte count was less than 11,000/mm^3 in 65% patients while, 35% patients had counts above 11,000/mm^3.

Of the 100 patients, 91% were diagnosed as acute appendicitis clinically while 9% were diagnosed with Appendicular perforation. On Ultrasonography, 82% patients were diagnosed with acute appendicitis or appendicular perforation while 18% had normal findings. Post-operatively 81% were confirmed as acute appendicitis while 19% were diagnosed with Appendicular perforation.

The mean bilirubin levels in patients diagnosed with acute appendicitis was 1.4 ±0.65 mg/dL (range, 0.75 – 2.05 mg/dL) while in patients diagnosed with Appendicular perforation was 1.9±1.16 mg/dL (range, 0.74 – 3.06 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with acute appendicitis was 0.9±0.57 mg/dL and 0.5±0.21 respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with Appendicular perforation was 1.2±1.06 mg/dL and 0.70±0.33 mg/dL respectively.

58 patients (71.6%) of the total patients diagnosed with acute appendicitis (n=81) were found to have elevated bilirubin levels while 23 patients (28.4%) had normal bilirubin levels. Similarly, 16 patients (84.21%) of the total patients diagnosed with Appendicular

perforation (n=19) were found to have elevated bilirubin levels while 03 patients (15.79%) had normal bilirubin levels.

The Sensitivity and Specificity of serum bilirubin as a marker in predicting acute appendicitis and Appendicular perforation was 71.6% and 15.79% respectively. Similarly the Positive predicative value and Negative predicative value for the same was 78.38% and 11.54% respectively with odds ratio 0.472.

Serum bilirubin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis is essentially still - clinical. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia double the normal range (Raise in Direct Bilirubin being still higher) should be identified as having a higher probability of Appendicular perforation suggesting, serum bilirubin levels have a predictive potential for the diagnosis of Appendicular perforation.

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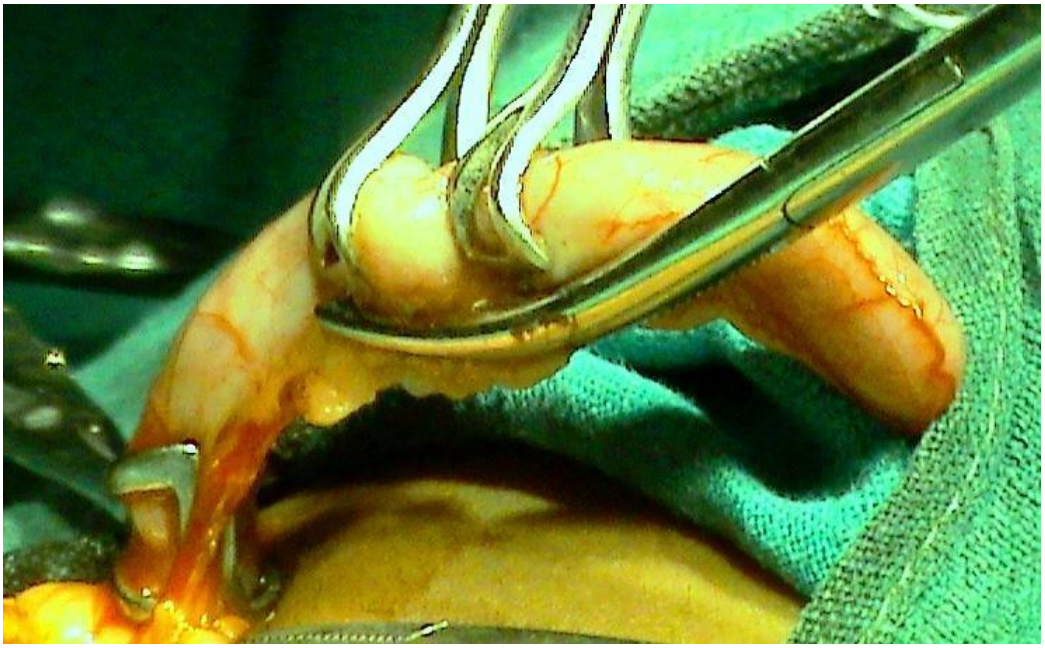
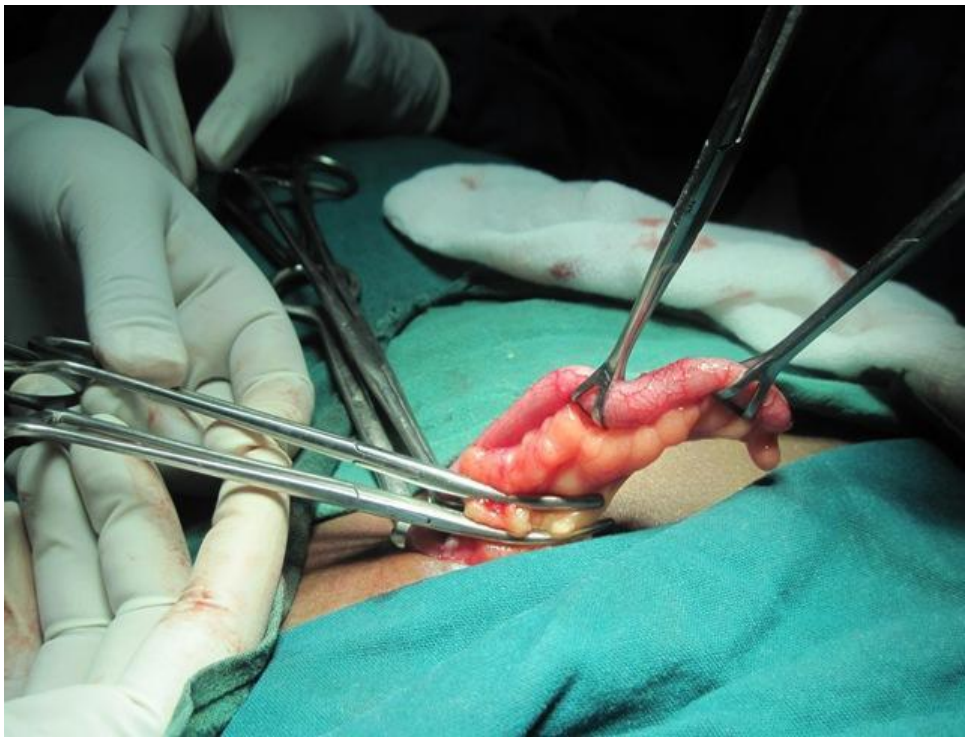
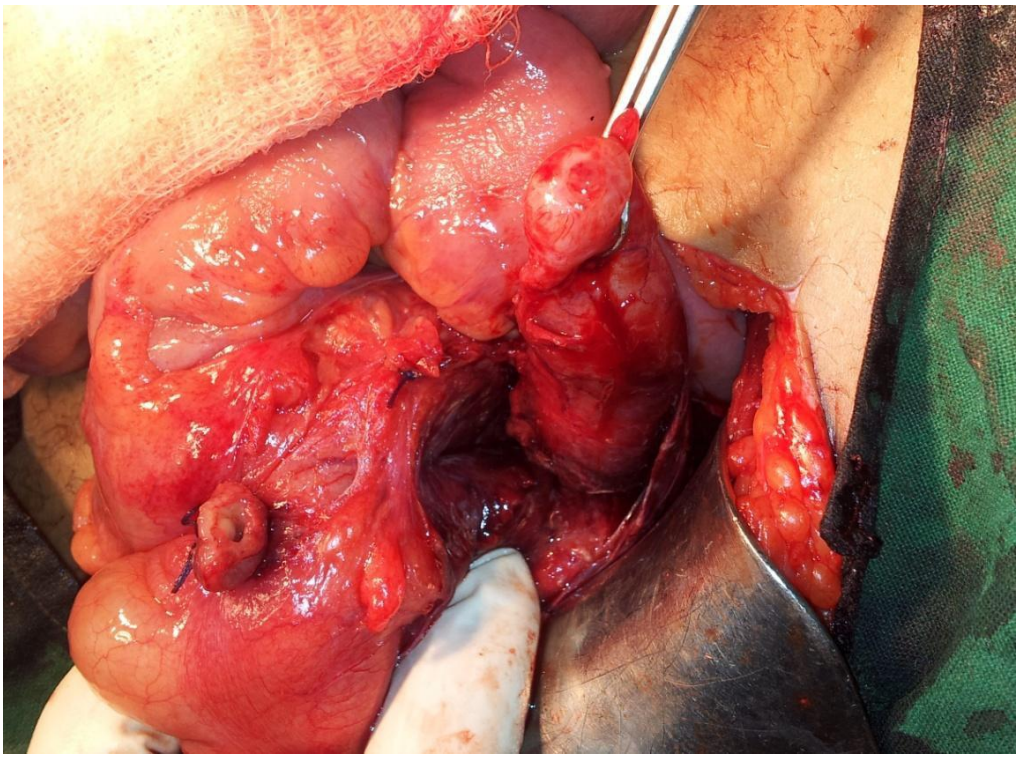


Photograph 1: Acute Appendicitis



Photograph 2. Acute appendicitis (mesoappendix being ligated)

Photograph 3: Inflamed Appendix with Faecalith



Photograph 4: Appendicular perforation (ligated and cut at base)

Annexures

Informed Consent

Name: Age/ Sex: IP:

I herewith declare that I have been explained in a language fully understood by me regarding the purpose of this study, methodology, proposed intervention, plausible side effects, if any and sequelae.

I have been given an opportunity to discuss my doubts and I have received the appropriate explanation.

I understand that my participation in this study is completely voluntary and that I am free to withdraw from this study at anytime without any prior notice &/ or without having my medical or legal rights affected.

I permit the author and the research team full access to all my records at any point, even if I have withdrawn from the study. However my identity will not be revealed to any third party or publication.

I herewith permit the author and the research team to use the results and conclusions arising from this study for any academic purpose, including but not limited to dissertation/ thesis or publication or presentation in any level.

Therefore, in my full conscience, I give consent to be included in the study and to undergo any investigation or any intervention therein.

Patient's Sign Investigator's Sign

(Dr.CHANDRASEKARAN.D)

"**EVALUATION OF HYPERBILIRUBINEMIA AS A NEW DIAGNOSTIC MARKER FOR ACUTE APPENDICITIS AND ITS ROLE IN THE PREDICTION OF APPENDICULAR PERFORATION"**

Investigator: **Dr.CHANDRASEKARAN.D** , PGY3 – MS (Gen Surg)

Guide: **Prof. Dr.R.V.SURESH MS**

- NAME : SL. NO:
- AGE /SEX:
- ADDRESS WITH CONTACT NUMBER:
- IP NO:
- DATE OF ADMISSION:
- DATE OF SURGERY:

:

HISTORY OF PRESENTING ILLNESS:

Pain :

duration ,

location ,

character

Vomiting:

onset :

duration:

Nausea

Anorexia

Fever

Diarrhoea

Any other relevant history

PAST HISTORY:

whether a known case of dm/hypertension/asthma/tb/epilepsy/cardiac illness

H/O jaundice/liver disease/hemolytic disorders

GENERAL EXAMINATION:

TEMP:

P.R:

B.P:

R.R

SYSTEMIC EXAMINATION:

CVS

RS

PER ABDOMEN:

PER RECTAL

CLINICAL DIAGNOSIS:

Investigations:

HEMAT		**LFT**	
HB		T.BIL	
PCV		D.BIL	
RBC			
TC			
DC			
PLT			
ESR			
RBS & ELECTROLYTE			

CHEST X RAY :

ABD X RAY:

USG ABD:

PATIENT CLINICAL COURSE:

OUTCOME OF TREATMENT:

Information Module

You are being invited to be a subject in this study.

Before you participate in this study, I am giving you the following details about this trial, which includes the aims, methodology, intervention, possible side effects, if any and outcomes:

All patients diagnosed with acute appendicitis on clinical examination and imaging will be included in this study. A detailed clinical history will be taken following a standardized proforma. A detailed clinical examination will be made and relevant investigations, basic and special investigations will be done at the time of admission.Bilirubin level and USG abdomen will be done at the time of admission. The prevalence of hyperbilirubinemia in acute appendicitis will be analysed. The results arising from this study will be analyzed and use for academic purposes. You will be given clear instructions at every step and you are free to ask/ clarify any doubts. Your identity will remain confidential. You are free to withdraw from this trial at any point of time, without any prior notice &/ or without any medical or legal implications.

I request you to volunteer for this study.

Thanking You,

(Dr.CHANDRASEKARAN.D) Name:

Serial Number	NAME	In Patient (IP) Number	Gender	Age	Liver function tests						TLC (/cmm3)	DLC				Clinical Diagnosis on	Ultra - Sonogra	Per-	Post-
					Total Biliru	Direct Biliru	Indirect	SGOT	SGPT	ALP		Neutrop	Lymphoc	Eosinoph	Monocyt				
1	Sathis	1450365	M	14	0.6	0.3	0.3	46	13	112	14300	89	7	4	0	AA	AA	AA	A
2	Ravi	26035	M	27	1.1	0.4	0.7	22	43	83	8200	75	20	2	3	AA	N	AA	A
3	Sullu	26098	M	22	0.8	0.2	0.6	91	26	100	9900	85	7	6	2	AA	AA	AA	A
4	Sivasankari	1448142	F	27	1.2	0.8	0.4	16	26	56	12200	57	40	3	0	AA	AA	AA	A
5	Venketesan	144810	M	29	1.4	0.9	0.5	35	12	93	6700	63	27	8	2	AA	AA	AA	A
6	Veeraragavan	260534	M	28	2.9	2.2	0.7	46	22	106	9300	87	12	1	0	AP	N	AP	A
7	Rajalakshimi	1448209	F	32	1.2	0.8	0.4	12	24	110	10900	64	28	6	2	AA	AA	AA	A
8	Sathya	1448207	F	14	1.4	1.2	0.2	34	12	76	8600	66	24	6	4	AA	AA	AA	A
9	Kalaiselvi	1448212	F	15	1.5	1.1	0.4	38	12	117	12300	78	13	7	2	AA	AA	AA	A
10	Shanawash	1448060	M	13	1.4	1.0	0.4	10	35	22	6300	58	40	2	0	AA	N	AA	A
11	Vanitha	1448240	F	16	4.4	3.4	1.0	25	39	54	10500	86	12	1	1	AA	AP	AP	A
12	Arun	1444007	M	18	0.8	0.2	0.6	34	29	92	2300	58	32	7	3	AA	AA	AA	A
13	Kowsalya	1448869	F	30	1.1	0.7	0.4	34	26	78	8600	55	42	2	1	AP	AA	AP	A
14	Senthil	1448209	M	29	0.9	0	1	18	16	45	14100	90	8	2	0	AA	AA	AA	A
15	Manimaran	1442977	M	20	0.9	0.2	0.7	32	11	77	7400	59	37	4	0	AA	AA	AA	A
16	Ganesan	20952	M	39	1.6	1.2	0.4	29	17	74	14200	85	13	2	0	AA	AA	AP	A
17	Jeejibai	20903	F	24	1.7	1.3	0.4	25	25	29	6900	71	29	0	0	AA	AA	AA	A
18	Kalaiarasan	21051	M	14	1.3	1.1	0.2	38	29	81	8100	54	44	1	1	AA	AP	AP	A
19	Shylash	21046	M	27	0.9	0.3	0.6	24	23	100	9900	58	40	2	0	AA	N	AA	A
20	Lalitha	20929	F	14	3.2	2.5	0.7	14	15	59	15500	80	18	2	0	AP	AP	AP	A
21	Saranya	21024	F	23	1.0	0.3	0.7	29	31	94	8200	50	47	2	1	AA	AA	AP	A
22	Shanthi	21222	F	40	1.4	1.2	0.2	33	11	72	9900	80	18	2	0	AA	AA	AA	A
23	Manjula	22114	F	17	1.2	0.3	0.9	25	14	67	12400	66	30	1	3	AA	AA	AA	A
24	Thangamani	21798	F	17	0.6	0.5	0.1	40	29	81	9500	60	30	#	0	AA	N	AA	A
25	Manjula	22114	F	18	1.4	1.1	0.3	34	12	81	12700	86	8	5	1	AA	N	AA	A
26	Usha	21983	F	11	1.6	1.2	0.4	19	22	71	10400	60	40	0	0	AA	AA	AA	A
27	Arunkumar	21983	M	16	4.2	3.8	0.4	22	12	80	12500	64	26	6	4	AP	AP	AP	A
28	Balaji	22035	M	22	1.3	0.9	0.4	34	12	96	4400	76	18	4	2	AA	N	AA	A
29	Kodiswaren	22071	M	27	1.1	0.8	0.3	22	34	30	10000	68	30	1	1	AA	AA	AA	A
30	Pushparaj	22104	M	45	0.6	0.3	0.3	18	18	98	16700	65	25	8	2	AP	AP	AP	A
31	Mani	20227	M	30	2.8	2.1	0.7	26	33	68	13300	74	20	4	2	AP	AP	AP	A
32	Maragatham	21957	F	25	2.0	1.2	0.8	30	94	130	9860	88	11	1	0	AA	AA	AP	A
33	Suryakumari	22065	F	41	1.4	0.7	0.7	30	48	110	11300	85	10	4	1	AA	AA	AA	A
34	Thyagu	22108	M	25	0.8	0.3	0.5	38	44	120	10250	65	30	5	0	AA	AA	AA	A
35	Valli	22896	F	23	0.9	0.4	0.5	18	34	44	14000	80	18	1	1	AA	AA	AA	A
36	Uma	1443143	F	10	2.3	1.5	0.8	24	32	100	4800	55	40	3	2	AA	AA	AP	A
37	Jothi	22036	F	25	1.1	0.6	0.5	27	22	65	9800	45	50	5	0	AA	N	AA	A

38	Nadhiya	23400	F	14	1.4	0.8	0.6	22	32	56	12000	88	10	1	1	AA	N	AA	AA
39	Ganesan	23141	M	10	1.0	0.3	0.7	25	34	70	2300	80	20	0	0	AA	AA	AA	AA
40	Nasrin	20600	F	17	1.4	1.0	0.4	32	14	56	15400	76	22	3	1	AA	AA	AA	AA
41	Jasmin	23185	F	25	0.7	0.5	0.2	24	20	92	16700	65	25	8	2	AA	AA	AA	AA
42	Kuppan	23155	M	16	2.8	2.1	0.7	26	33	68	13300	80	15	4	1	AA	AA	AA	AA
43	Venketesan	22870	M	26	2.0	1.4	0.6	12	15	110	9800	88	11	1	0	AA	N	AA	AA
44	Manjula	23368	M	30	0.7	0.4	0.3	34	18	90	11300	85	10	4	1	AA	N	AA	AA
45	Murugavalli	22577	F	18	1.7	1.2	0.5	31	12	90	10250	65	30	5	0	AA	AA	AA	AA
46	Ravi	26085	M	38	1.4	0.4	1.0	35	28	90	14000	80	18	1	1	AA	AP	AP	AP
47	Ganesan	26112	M	45	2.2	0.8	1.4	40	38	90	14800	85	10	3	2	AA	AP	AP	AP
48	Sillu	26098	M	35	1.1	0.6	0.5	27	22	65	9800	45	50	5	0	AA	AP	AP	AP
49	Durai	26002	M	12	0.9	0.2	0.7	15	22	110	12000	88	10	1	1	AP	AP	AP	AP
50	Mari	14272280	M	35	1.0	0.3	0.7	25	34	70	2300	80	20	0	0	AA	AA	AA	AA
51	Samantha rani	25798	F	28	1.4	1.0	0.4	32	14	56	15400	76	20	3	1	AA	AA	AA	AA
52	Raman	27007	M	13	1.6	1.4	0.2	38	27	86	5000	60	38	2	0	AA	AA	AA	AA
53	Rasith	27253	M	33	2.5	2.2	0.3	21	33	45	11200	77	13	7	3	AA	AA	AA	AA
54	Shyla	26039	F	60	0.8	0.6	0.2	32	13	55	8400	78	20	1	1	AA	N	AA	AA
55	Suganthi	25098	F	18	1.1	0.9	0.2	12	33	80	12800	50	40	9	1	AA	AA	AA	AA
56	Madheena beevi	25974	F	13	2.1	1.5	0.6	35	25	90	7500	80	20	0	0	AA	AA	AA	AA
57	Chandra	27293	F	25	0.7	0.5	0.2	28	32	80	3500	65	30	5	0	AA	AA	AA	AA
58	Lakshimi	27452	F	28	3.2	2.0	1.2	29	21	33	18000	70	28	1	1	AA	N	AA	AA
59	Shalini	27650	F	15	1.4	0.9	0.5	26	24	65	9800	80	18	1	1	AA	AA	AA	AA
60	Uma maheshwari	27379	F	20	1.9	1.3	0.6	34	34	98	11000	60	30	8	2	AA	AA	AA	AA
61	Kishore kumar	27281	M	28	1.8	1.2	0.6	40	29	87	6700	65	35	0	0	AA	N	AA	AA
62	Sathiskumar	28978	M	20	1.2	1.0	0.2	25	35	65	9900	88	10	2	0	AA	AA	AA	AA
63	Prasanth	29680	M	60	1.2	0.6	0.6	19	21	47	6750	80	16	3	1	AA	AA	AA	AA
64	Suresh	29198	M	12	1.3	0.9	0.4	33	24	88	12000	78	20	2	0	AP	AP	AP	AP
65	Sakthivel	29227	M	9	1.5	0.6	0.9	20	13	24	6700	60	38	1	1	AA	AA	AA	AA
66	Shyamala	27342	F	22	1.6	1.0	0.6	35	34	65	3400	50	46	4	0	AA	N	AA	AA
67	Rekha	29140	F	12	2.0	1.2	0.8	16	34	120	18450	70	22	6	2	AA	AA	AA	AA
68	Mohammed rafi	29207	M	55	1.9	1.3	0.6	34	28	45	5600	66	30	4	0	AA	AA	AA	AA
69	Suresh kumar	29210	M	20	3.5	2.7	0.8	33	55	78	22540	78	21	1	0	AA	AA	AA	AA
70	Udhayakumari	29234	F	35	1.5	1.2	0.3	23	34	67	7500	60	30	8	2	AA	AA	AA	AA
71	Arumugam	29088	M	17	1.1	0.6	0.5	12	23	56	9000	75	20	2	3	AA	N	AA	AA
72	Silambarasan	29223	M	8	1.3	0.9	0.4	21	34	46	8000	67	30	3	0	AA	AA	AA	AA
73	Aravind	28646	M	13	1.4	1.0	0.4	14	14	76	7600	78	22	0	0	AA	AA	AA	AA
74	Prasanna	28826	M	30	0.8	0.6	0.2	32	21	64	9000	50	40	#	0	AA	AA	AA	AA
75	Anand	28535	M	28	1.7	0.7	1.0	34	34	76	8500	80	18	2	0	AA	AA	AA	AA
76	Nagaraj	28968	M	38	0.6	0.5	0.1	34	23	76	10500	76	20	3	1	AA	AA	AA	AA
77	Sangeetha	28931	F	30	1.4	1.2	0.2	22	32	48	7000	55	35	8	2	AA	N	AA	AA
78	Raja	28976	M	21	2.9	2.0	0.9	25	32	88	13100	68	30	0	2	AA	AA	AA	AA

79	Babu	1441436	M	8	3.9	3.0	0.9	26	13	132	9000	80	16	4	0	AA	AA	AA	A
80	Sasi	1441420	M	20	2.3	1.6	0.7	21	19	100	14500	82	16	1	1	AA	AA	AA	A
81	Karthick	1441460	M	18	0.9	0.2	1	20	23	106	4800	67	20	3	0	AA	AA	AA	A
82	Revathi	1441465	F	22	1.2	0.2	1	12	22	89	6400	83	10	5	2	AA	AP	AP	A
83	Chellamma	1441463	F	70	1.3	0.9	0	10	10	113	13800	88	8	2	2	AA	AA	AA	A
84	Chandru	1443257	M	15	0.9	0.3	1	23	21	67	4400	80	12	6	2	AA	AA	AA	A
85	Manikandan	1445064	M	32	1.3	1.1	0	24	32	99	8000	67	29	3	1	AA	AA	AA	A
86	Vijay	1443879	M	18	1.6	1.2	0	12	34	110	9400	80	12	6	2	AA	AA	AA	AA
87	Narain	1443865	M	20	1.8	1.3	0.5	22	35	100	8300	58	29	9	4	AA	AA	AA	A
88	Saravanan	1443783	M	19	0.6	0.2	0.4	18	17	110	8600	64	30	5	1	AA	N	AA	A
89	Rameshkumar	1443663	M	26	1.4	1.2	0.2	32	25	111	15000	90	6	3	1	AA	AA	AA	A
90	Keerthivasan	1443628	M	12	1.3	0.5	0.8	26	39	91	4500	69	27	4	1	AP	AP	AP	A
91	Saraswathi	1441462	F	12	1.7	1.2	0.5	19	25	56	6900	63	32	4	1	AA	AA	AA	A
92	Saroja	1441549	F	28	0.9	0.3	0.6	34	46	120	14300	89	7	4	0	AA	AA	AA	A
93	Shathi	1441550	F	15	1.1	0.4	0.7	22	43	83	8200	75	20	5	0	AA	AA	AA	A
94	Farook	1445893	M	16	0.8	0.2	0.6	91	26	100	9900	85	7	6	2	AA	AA	AA	A
95	Madhavan	1443891	M	11	1.2	0.8	0.4	16	26	56	12200	57	40	2	1	AA	AA	AA	A
96	Priyanka	1441492	F	12	1.4	0.9	0.5	35	12	93	6700	63	29	8	0	AA	AA	AA	AA
97	Geetha	1444293	F	10	0.9	0.2	0.7	46	22	106	9300	87	12	1	0	AA	AA	AA	A
98	Gunasekaran	1443973	M	21	2.2	1.8	0.4	12	24	110	10000	64	28	6	2	AA	AA	AA	A
99	Soundarya	1444009	F	14	1.4	1.2	0.2	34	12	76	8600	66	27	5	2	AA	AA	AA	A
100	Vijayarai	1444151	M	24	1.5	1.1	0.4	38	12	117	12500	78	14	6	2	AA	AA	AA	A

KEY TO MASTER CHART

AA - Acute appendicitis

ALP - Alkaline phosphatase

AP - Appendicular perforation

dL - Deciliters

DLC - Differential leukocyte count

F - Female

M - Male

mg - Milligrams

mm - Millimeters

N - Normal

SGOT - Serum glutamic oxaloacetic transaminase

SGPT - Serum glutamic pyruvic transaminase

TLC - Total leukocyte count

"EVALUATION OF HYPERBILIRUBINEMIA AS A NEW DIAGNOSTIC MARKER FOR ACUTE APPENDICITIS AND ITS ROLE IN THE PREDICTION OF APPENDICULAR PERFORATION"